STN TRANSCRIPT FOR 10/524,517

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NEWS 2	MAR 15	WPIDS/WPIX enhanced with new FRAGHITSTR display format
NEWS 3	MAR 16	CASREACT coverage extended
NEWS 4	MAR 20	MARPAT now updated daily
NEWS 5	MAR 22	LWPI reloaded
NEWS 6	MAR 30	RDISCLOSURE reloaded with enhancements
NEWS 7	APR 02	JICST-EPLUS removed from database clusters and STN
NEWS 8	APR 30	GENBANK reloaded and enhanced with Genome Project ID field
NEWS 9	APR 30	CHEMCATS enhanced with 1.2 million new records
NEWS 10	APR 30	CA/CAplus enhanced with 1870-1889 U.S. patent records
NEWS 11	APR 30	INPADOC replaced by INPADOCDB on STN
NEWS 12	MAY 01	New CAS web site launched
NEWS 13	MAY 08	CA/CAplus Indian patent publication number format defined
NEWS 14	MAY 14	RDISCLOSURE on STN Easy enhanced with new search and display fields
NEWS 15	MAY 21	BIOSIS reloaded and enhanced with archival data
NEWS 16	MAY 21	TOXCENTER enhanced with BIOSIS reload
NEWS 17	MAY 21	CA/CAplus enhanced with additional kind codes for German patents
NEWS 18	MAY 22	CA/CAplus enhanced with IPC reclassification in Japanese patents
NEWS 19	JUN 27	CA/CAplus enhanced with pre-1967 CAS Registry Numbers
NEWS 20	JUN 29	STN Viewer now available
NEWS 21	JUN 29	STN Express, Version 8.2, now available
NEWS 22	JUL 02	LEMBASE coverage updated
NEWS 23	JUL 02	LMEDLINE coverage updated
NEWS 24	JUL 02	SCISEARCH enhanced with complete author names
NEWS 25	JUL 02	CHEMCATS accession numbers revised
NEWS 26	JUL 02	CA/CAplus enhanced with utility model patents from China
NEWS 27	JUL 16	CAplus enhanced with French and German abstracts
NEWS 28	JUL 18	CA/CAplus patent coverage enhanced

NEWS EXPRESS 29 JUNE 2007: CURRENT WINDOWS VERSION IS V8.2,
CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
AND CURRENT DISCOVER FILE IS DATED 05 JULY 2007.

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NEWS LOGIN	Welcome Banner and News Items
NEWS IPC8	For general information regarding STN implementation of IPC 8

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* * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 13:14:45 ON 24 JUL 2007

=> file reg

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STRUCTURE FILE UPDATES: 23 JUL 2007 HIGHEST RN 943188-87-2
DICTIONARY FILE UPDATES: 23 JUL 2007 HIGHEST RN 943188-87-2

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http://www.cas.org/support/stngen/stndoc/properties.html

=>
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chain nodes :

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7  8  9  11  12  14  15
ring nodes :
1  2  3  4  5  6
chain bonds :
1-7  2-14  3-15  5-11  6-12  7-8  7-9
ring bonds :
1-2  1-6  2-3  3-4  4-5  5-6
exact/norm bonds :
1-2  1-6  1-7  2-3  2-14  3-4  3-15  4-5  5-6  5-11  6-12  7-8  7-9
isolated ring systems :
containing 1 :


G1:C,H,O,X

Match level :
1:Atom  2:Atom  3:Atom  4:Atom  5:Atom  6:Atom  7:CLASS  8:CLASS  9:CLASS  11:CLASS
 12:CLASS  14:CLASS  15:CLASS



L1      STRUCTURE UPLOADED

=> d l1
L1 HAS NO ANSWERS
L1                STR
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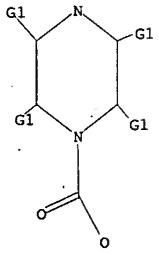


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G1 C,H,O,X


Structure attributes must be viewed using STN Express query preparation.


=> s l1
SAMPLE SEARCH INITIATED 13:16:36 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -    3333 TO ITERATE

 60.0% PROCESSED     2000 ITERATIONS                          50 ANSWERS
INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:        63198 TO    70122
PROJECTED ANSWERS:           35865 TO    41127

L2           50 SEA SSS SAM L1

=> s l1 sss full
FULL SEARCH INITIATED 13:16:51 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -    66728 TO ITERATE

100.0% PROCESSED    66728 ITERATIONS                     38680 ANSWERS
SEARCH TIME: 00.00.01

L3        38680 SEA SSS FUL L1

=> file caplus
COST IN U.S. DOLLARS                        SINCE FILE     TOTAL
                                              ENTRY     SESSION
FULL ESTIMATED COST                          173.00     173.21

FILE 'CAPLUS' ENTERED AT 13:17:17 ON 24 JUL 2007
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FILE COVERS 1907 - 24 Jul 2007  VOL 147 ISS 5
FILE LAST UPDATED: 23 Jul 2007  (20070723/ED)

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http://www.cas.org/infopolicy.html

=> s l3
L4         7821 L3

=> s l3/prep
           7821 L3
        4435862 PREP/RL
L5         5822 L3/PREP
                (L3 (L) PREP/RL)

=> s l5 and water
        2561153 WATER
         265715 WATERS
        2618195 WATER
                (WATER OR WATERS)
L6          158 L5 AND WATER

=> s l6 and (oxycarbon? or carboxy or carboxyl)
           2943 OXYCARBON?
          75712 CARBOXY
          74338 CARBOXYL
            749 CARBOXYLS
          74753 CARBOXYL
                (CARBOXYL OR CARBOXYLS)
L7            7 L6 AND (OXYCARBON? OR CARBOXY OR CARBOXYL)

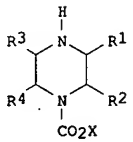
=> d l-7 ibib abs

L7   ANSWER 1 OF 7  CAPLUS  COPYRIGHT 2007 ACS on STN
```

ACCESSION NUMBER: 2004:326428 CAPLUS
DOCUMENT NUMBER: 140:357373
TITLE: Purification piperazine derivatives
INVENTOR(S): Morimoto, Masao; Sato, Haruyo
PATENT ASSIGNEE(S): Toray Fine Chemical K. K., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 22 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2004123629	A	20040422	JP 2002-291344	20021003

PRIORITY APPLN. INFO.: JP 2002-291344 20021003
OTHER SOURCE(S): MARPAT 140:357373
GI



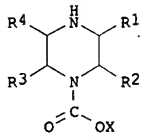
I

AB Piperaine derivs. I (R1, R2, R3, R4 = H, alkyl, alkoxy, halo, carboxyl, carbamoyl, alkylcarbamoyl; X = alkyl, alkenyl, alkynylaralkyl, alkoxyaryl; except R1-R4 = H) were purified by dissolved the crude compds. in water at pH ≤ 3 at 20° and washed with organic solvent having <10 wt% mutual solubility, or by distillation Thus, 2-methylpiperazine was treated with benzyl chlorocarbonate in BuOH at 0° for 2 h, and BuOH was remover by distillation, water and 35% HCl was added to adjusted pH to 0.8, washed with toluene several times to give, after treatment with 48% aqueous NaOH to pH 11.5, 1-benzyloxycarbonyl-3-methylpiperazine.

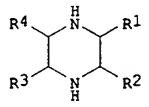
L7 ANSWER 2 OF 7 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:220323 CAPLUS
DOCUMENT NUMBER: 140:253580
TITLE: Process for producing oxycarbonyl -substituted piperazine derivative
INVENTOR(S): Morimoto, Masao; Sato, Haruyo
PATENT ASSIGNEE(S): Toray Fine Chemicals Co,. Ltd., Japan
SOURCE: PCT Int. Appl., 54 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004022548	A1	20040318	WO 2003-JP11204	20030902
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR,				
TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2003264365	A1	20040329	AU 2003-264365	20030902
EP 1548010	A1	20050629	EP 2003-794183	20030902
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
CN 1681797	A	20051012	CN 2003-821231	20030902
JP 2004115510	A	20040415	JP 2003-314809	20030905
US 2006161003	A1	20060720	US 2005-524517	20050211

PRIORITY APPLN. INFO.: JP 2002-260376 A 20020905
WO 2003-JP11204 W 20030902
OTHER SOURCE(S): CASREACT 140:253580; MARPAT 140:253580
GI



I



II

AB Disclosed is a process for producing an oxycarbonyl-substituted piperazine derivative [I; R1-R4 = H, C1-4 alkyl, C1-4 alkoxy, halo, CO2H, CONH2, C1-4 alkylcarbamoyl; X = C1-4 alkyl, C2-4 alkenyl, C2-4 alkynyl, (un)substituted aralkyl or aryl; wherein a compound represented by R1-R4 = H is excluded] from a piperazine derivative (II; R1-R4 = same as above), wherein the piperazine derivative is oxycarbonylated by the use of an organic solvent whose water content is 15% or less. Thus, 2-methylpiperazine (5.00 g, 0.0499 mol)was dissolved in 44 g 1-butanol (0.05 weight% H2O content), cooled to 0°, treated dropwise with 10.1 g g benzyl chloroformate (0.0579 mol, 1.17 equiv)at 0-8°, and stirred at 0-5° for 2 h and at room temperature for 12 h to give 95.1% 1-benzyloxycarbonyl-3-methylpiperazine.
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 3 OF 7 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:58066 CAPLUS
DOCUMENT NUMBER: 138:112415
TITLE: Preparation of amide-containing oxazolidinones having improved solubility and bioavailability
INVENTOR(S): Hester, Jackson B., Jr.
PATENT ASSIGNEE(S): Pharmacia & Upjohn Company, USA
SOURCE: PCT Int. Appl., 331 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003006440	A2	20030123	WO 2002-US22526	20020712
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,				

PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,
UA, UG, US, UZ, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF,
CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CA 2452513	A1	20030123	CA 2002-2452513		20020712
AU 2002354579	A1	20030129	AU 2002-354579		20020712
US 2004014967	A1	20040122	US 2002-194914		20020712
US 7049443	B2	20060523			
EP 1451164	A2	20040901	EP 2002-752358		20020712
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE					
JP 2005520782	T	20050714	JP 2003-512212		20020712
MX 2004PA00357	A	20040504	MX 2004-PA357		20040112
PRIORITY APPLN. INFO.:			US 2001-304808P	P	20010712
			WO 2002-US22526	W	20020712

OTHER SOURCE(S): MARPAT 138:112415
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The present invention is directed to amide-containing oxazolidinones (1) which have an improved solubility (no data) and a method of improving the solubility of amide-containing oxazolidinone bactericides. A very broad range of compds. 1 is claimed (see claims for details). Also claimed is a method of conversion of amide-containing oxazolidinones to more water-soluble derivs. comprising reaction with 3-(2-((dipropoxyphosphinyl)oxy)-4,6-dimethylphenyl)-3-methylbutanoyl chloride to form a C(O)NRC(O) or C(O)NRC(S) linkage followed by deprotection to give a phosphoric acid monoester. However, the only example is somewhat different in that I is prepared starting from II and III, followed by N-acylation and hydrogenation. In addition to the presence of the phosphonooxy group in compds. 1, also claimed are compds. 1 containing an acyloxy group. The bioavailability of these oxazolidinones is improved by improving the solubility thereof. Also included in the examples are prepns. of .apprx.25 amide-containing oxazolidinones, from which compds. 1 can potentially be prepared

L7 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1968:78768 CAPLUS
DOCUMENT NUMBER: 68:78768
TITLE: Acetylenically unsaturated polyesters, polycarbonates, and polyurethanes
PATENT ASSIGNEE(S): Union Carbide Corp.
SOURCE: Brit., 16 pp.
CODEN: BRXXAA
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
GB 1103305		19680214	GB 1965-5839	19650210
US 3380965		19680430	US 1964-343453	19640210
US 3484411		19691216	US	19670410
PRIORITY APPLN. INFO.:			US	19640210

GI For diagram(s), see printed CA Issue.
AB The synthesis of acetylenically unsatd. polyesters, polycarbonates, and polyurethanes having very useful phys. properties and heat stability at ≤300° is described. The polyesters are prepared by condensation of an acetylenic diol with a diacyl halide at 30-180° in an aromatic or chlorinated aliphatic hydrocarbon solvent, the polycarbonates are obtained by the base-catalyzed interfacial polycondensation of an acetylenic diol with a dihaloformate at -10 to +50° in an aromatic or chlorinated aliphatic hydrocarbon, and the polyurethanes are prepared by the interfacial condensation of an acetylenic glycol dihaloformate with a secondary amine. Thus, 0.86 g. 2-butyne-1,4-diol (I), 2.03 g. isophthaloyl chloride, and 15 ml. sym-tetrachloroethane was refluxed 27 hrs. under argon, the viscous residue dissolved in 50 ml. CHCl3, and the solution filtered through Celite and added to 500 ml. iso-PrOH to give a 75% yield of white, fibrous polyester having a reduced sp. viscosity of 0.75 at 25° and forming a film having a glass-transition temperature of 50°, m.p. 100°, tensile modulus 35,000 psi., tensile strength 3200 psi., and crystallinity 30%. Similarly prepared was a 1,4-cis-cyclohexanedicarboxylic acid-I polyester and a terephthalic acid-3-hexyne-2,5-diol polyester. N,N-Dimethylaniline (48.4 g.) in 100 ml. CH2Cl2 was added during 21 min. at 5-13° to 17.2 g. I, 300 ml. CH2Cl2, and 30.7 ml. liquid COCl2, the mixture stirred 30 min. and devolatilized under vacuum at 30-5°, the residue extracted with 400 ml. Et2O, the organic extract filtered through Celite and evaporated, and the residue dissolved in C6H6 and filtered through magnesia-silica to give 2-butyne-1,4-diol dichloroformate (II), b0.4-0.6 85-92°, nD25 1.4770. II (2.11 g.) in 30 ml. CH2Cl2 was added during 12 min. to 3.24 g. α-bisphenol (III), 1 g. NaOH, 50 ml. H2O, 5 drops Et3N, and 30 ml. CH2Cl2, the mixture stirred for 20 min. with the addition of 5 more drops Et3N, the organic layer washed with H2O and then with 400 ml. H2O containing 3 ml. concentrated H3PO4, the aqueous layer of pH 1.4 washed with water until pH 5-7, and the organic layer added to 600 ml. iso-PrOH to give an 80% yield of white, fibrous polycarbonate having a reduced sp. viscosity of 0.99 at 25°. Similarly prepared were bisphenol A-bisphenol A dichloroformate-II polycarbonate, polycarbonates from II and bisphenol A, 1,3-bis(p-hydroxyphenyl)-1-ethylcyclohexane, α-bisphenol, 2,2-bis(2,3,4,6-tetrachloro-4-hydroxyphenyl)propane, acetophenone bisphenol, 2,2-bis(2,6-dichloro-4-hydroxyphenyl)propane, cyclohexanone bisphenol, bis(4-hydroxyphenyl) sulfone, bisphenol of 1,4-dimethylenecyclohexane, bisphenol of α,α'-dichloro-p-xylene, bisphenol bis(chloromethyl)durene, β-bisphenol (IV)-γ-bisphenol (V), and bisphenol A-1,4-diphenol-2-butyne-1,4-diol dichloroformate polycarbonate. Treatment of 1.14 g. trans-2,5-dimethylpiperazine (VI), 15 ml. H2O, 1 g. NaOH, 3 drops Et3N, and 20 ml. CH2Cl2 with 2.11 g. II in 20 ml. CH2Cl2 gave a 96.8% yield of a polyurethane having a softening point of 75° and a reduced viscosity of 0.28. Similarly prepared were poly(carbonate urethanes) from II, VI, and bisphenol A, β-bisphenol-γ-bisphenol, or 1,3-bis(p-hydroxyphenyl)-1-ethylcyclohexane.

L7 ANSWER 5 OF 7 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1966:104252 CAPLUS
DOCUMENT NUMBER: 64:104252
ORIGINAL REFERENCE NO.: 64:19625a-f
TITLE: Dithiocarboxylated cephalosporins
INVENTOR(S): Heyningen, Earle Van; Brown, Carter N.
PATENT ASSIGNEE(S): Eli Lilly & Co.
SOURCE: 5 pp.
DOCUMENT TYPE: Patent
LANGUAGE: Unavailable
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 3239516		19660308	US 1965-426392	19650118

NL 6600248 NL
PRIORITY APPLN. INFO.: US 19650118
GI For diagram(s), see printed CA Issue.
AB The preparation is described of the title compds. (I) and betaines (II), which show resistance to the destructive action of penicillinase and have a high degree of activity against a broad range of both gram-pos. and gram-neg. pathogens. Thus, 0.0012 mole Na 7-acylamidocephalosporanate and an equimolar amount of Na piperazinodithiocarboxylate (III) were dissolved in 10 ml. H2O, the mixture heated at 40-5° for 24 hrs., and filtered. From the filtrate was precipitated a yellow glass by addition of an equal volume of aqueous saturated NaCl solution and chilling for several hrs. The supernatent solution was decanted and the solid dissolved in 25-50 ml. CHCl3. The CHCl3 solution was washed with 50% saturated aqueous NaCl solution, evaporated to half its volume, diluted with Et2O and chilled to give I. The I (R1 = α-thienyl) prepared were (R2 and % yield given): Me, 23.5; Et, 6.1; Pr, 25.2; iso-Pr, 13.3; Bu, 23.2; amyl, 14.2; β-hydroxyethyl, 9.6. Other I prepared were α-thienylmethyl 2- carboxy-4-methylpiperazinodithiocarboxyl ate cephalosporin and phenylthiomethyl 4-methylpiperazinodithiocarboxylate cephalosporin. II were prepared by mixing a solution of 0.01 mole of the crude Na salt of I in 100 ml. dry CHCl3 with a solution of 0.0105 mole alkyl or alkenyl halide in 10 ml. CHCl3. The mixture was held at room temperature with occasional shaking for 4-7 days during which time a solid precipitated The precipitate was separated, air-dried, and triturated with water. The product was dissolved in HCON-Me2 (25-35 ml./g.) by warming gently and adding H2O until the cloudiness cleared. Tetrahydrofuran (5-10 vols.) was added, and the turbid mixture cooled to give II. The following II (R1 = α-thienyl, R2 = Me) were prepared (R3 and % yield given): Me, 48; Pr, 26.4; allyl 66.3; Bu, 25. The following III were also prepared in which the substituent at the 4 position of the piperazine ring is referred to as R2 (R2, m.p., and % yield given): Me, >290°, 45.5; Et, 232-5°, 76; Pr, 265-8°, 80; iso-Pr, 262-6°, 61.7; Bu, 248-50°, 63; amyl, 254-8°, 85. The uv spectra of I and II were recorded.

L7 ANSWER 6 OF 7 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1965:59429 CAPLUS
DOCUMENT NUMBER: 62:59429
ORIGINAL REFERENCE NO.: 62:10562c-e
TITLE: Monoazo dyes
INVENTOR(S): Wunderlich, Hermann; Wolfrum, Gerhard
PATENT ASSIGNEE(S): Farbenfabriken Bayer A.-G.
SOURCE: 16 pp.
DOCUMENT TYPE: Patent
LANGUAGE: Unavailable
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
BE 638210		19640203	BE	
PRIORITY APPLN. INFO.:			DE	19621005

GI For diagram(s), see printed CA Issue.
AB Dyes which are insol., or difficultly soluble, in water for dyeing and printing synthetic fibers, especially polyesters and cellulose esters, with the aid of dispersants, have the general formula I and are prepared by coupling a diazonium salt with a 1-acyl-4-phenylpiperazine derivative Thus, 2,4-Cl(O2N)C6H3NH2 (II) 2.7 was diazotized and coupled in AcOH 10 with N-methyl-4-(m-tolyl)-1-piperazinecarboxamide (III) 4.9 parts, m. 99° (from molar amts. of MeNCO and 1-(m-tolyl)piperazine (IV) in CH2Cl2 or C6H6 at 10° with slight heating in the absence of moisture) to give I (X = O2N, Y = Cl, Z = Me, R = CONHMe), a bluish red dye. Other I were similarly prepared (X, Y, Z, R, and shade given): O2N, H, Cl, Ac, orange; O2N, Cl, H, COC6H4OH-2, yellowish-red; Cl, O2N, H, COC6H3C12-2,4, yellowish red; O2N, Cl, H, CO2Et, yellowish red; O2N, Cl, H, COCH2Ac, red; O2N, CN, H, COCH2CH2Cl, bluish red; Cl, Cl, H, SO2Me, reddish yellow. Also prepared was 5-amino-3-phenyl-1,2,4-thiadiazole → N-dimethyl analog of III, red. Prepns. of the following 1-acylpiperazines are reported (acyl group and m.p. given): CONMe2, --; Ac, --; COC6H4OH-2, 163-4°; COC6H3C12-2,4, --; CO2Et, --; SO2Me, --; COCH2Ac, 50-1°; COCH2CH2Cl, 87-8°.

L7 ANSWER 7 OF 7 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1955:24199 CAPLUS
DOCUMENT NUMBER: 49:24199
ORIGINAL REFERENCE NO.: 49:4730i,4731a-i,4732a
TITLE: Amino piperazines
INVENTOR(S): Conroy, Edward A.; Parker, Robert P.
PATENT ASSIGNEE(S): American Cyanamid Co.
DOCUMENT TYPE: Patent
LANGUAGE: Unavailable
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2663707		19531222	US 1951-233126	19510622

GI For diagram(s), see printed CA Issue.
AB Substituted N-aminopiperazines having central nervous system depressant, anticonvulsant, sedative, anesthetic or analgesic action are prepared RN.CHY1.CH2.NNHZ.CHY2.CH2 (I), where Z=H, Y1 and Y2 = Me or H, R = alkyl, aralkyl, monocyclic aryl, carbalkoxy, di-alkylcarbamyl, or heterocyclic radical. In the product, Z is a carbalkoxy, carbamoyl, thiocarbamoyl, or acyl radical. Method 1. 1-Carbethoxy-4-aminopiperazine (II) 35 and NaHCO3 21 parts in absolute EtOH 80 parts stirred below 50° while a solution of EtO2CCl (III) 21.5 in absolute EtOH 80 parts is added, the mixture refluxed 2 h., filtered, and the EtOH evaporated give Et N-(4-carbethoxy-1-piperazyl)carbamate, m. 143.5-4.5° (from Et2O). Method 2. II 34.6, Ac2O 20.5, and AcOH 150 parts heated (water bath) for 30 min., then poured into water 500 and concentrated ammonia 180 parts, the solution extracted with CHCl3 and the CHCl3 evaporated gives 1-carbethoxy-4-acetamidopiperazine, m. 180.5-1.0° (from acetone). Method 3. Ph isocyanate (IV) 75 in Et2O 75 parts added to II 26 in Et2O 150 parts over 10 min. at ice-bath temperature and the mixture filtered gives 1-phenyl-3-(4-carbethoxy-1-piperazyl)urea, m. 143.5-4.5° (from Me2CO-hexane). Method 4. Benzoyl chloride 28.1 added (10 min.) to a solution of 1-diethylcarbamoyl-4-aminopiperazine (V) 37 in 5% aqueous NaOH 150 parts, the mixture extracted with CHCl3, the CHCl3 evaporated gives 1-diethylcarbamoyl-4-benzoylaminopiperazine, m. 111-12° (from Me2CO-Et2O). The following list of products was also prepared The method number, starting material, other reactant, solvent, product, m. or b.p. of product, and crystallization solvent are given. 1, II, PhCH2COCl (VI), benzene, 1-carbethoxy-4-phenylacetyl-aminopiperazine, m. 138-9°, EtOAc; 3, II, cyclohexyl isocyanate (VII), Et2O, 1-cyclohexyl-3-(4-carbethoxy-1-piperazyl)urea, m. 159.5-60.5°, Me2CO-hexane; 3, II, PhNCS, Et2O, 1-phenyl-3-(4-carbethoxy-1-piperazyl)thiourea, m. 189-90°, EtOH; 3, II, allyl isothiocyanate (VIII), Et2O, 1-allyl-3-(4-carbethoxy-1-piperazyl)thiourea, m. 132-3°, Me2CO-hexane; 1, V, III, EtOH, Et N-(4-diethylcarbamoyl-1-piperazyl)carbamate, b5.0 200-5°, -; 2, V, Ac2O, AcOH, 1-diethylcarbamoyl-4-acetylaminopiperazine, m. 85.5-6.5°, Me2CO-Et2O; 3, V, IV, Et2O, 1-phenyl-3-(4-diethylcarbamyl-1-piperazyl)urea, m. 111-13°, Me2CO-hexane; 3, V, VII, Et2O, 1-cyclohexyl-3-(4-diethylcarbamoyl-1-piperazyl)urea, m. 98.0-9.5°, hexane; 3, V, EtNCS (IX), Et2O, 1-ethyl-3-(4-diethylcarbamoyl-1-piperazyl)thiourea, m. 146-7°, Me2CO-hexane; 4,

V, 4-chlorobenzenesulfonyl chloride (X), 5% NaOH, N-(4-diethylcarbamoyl-1-piperazyl)-4-chlorobenzenesulfonamide, m. 150.5-1.5°, aqueous EtOH; 1, 1-methyl-4-aminopiperazine (XI), III, EtOH, Et N-(4-methyl-4-aminopiperazyl)carbamate, b3 122-4°; 3, XI, VII, Et2O, 1-cyclohexyl-3-(4-methyl-1-piperazyl)urea, m. 159.5-60.0°, Me2CO; 3, XI, IX, Et2O, 1-ethyl-3-(4-methyl-1-piperazyl)thiourea, m. 156.2-6.7°, Me2CO; 1, 1-benzyl-4-aminopiperazine (XII), III, EtOH, Et N-(4-benzyl-1-piperazyl)carbamate, m. 95.5-6.5°, hexane; 2, XII, Ac2O, AcOH, 1-benzyl-4-acetamidopiperazine, m. 136-7°, Me2CO; 4, XII, VI, benzene-pyridine, 1-benzyl-4-phenylacetamidopiperazine, m. 161.0-1.7°, Me2CO; 4, XII, BzCl, 5% NaOH, 1-benzyl-4-benzoylaminopiperazine, m. 173-4°, Me2CO; 3, XII, IV, Et2O, 1-phenyl-3-(4-benzyl-1-piperazyl)urea, m. 135.0-5.5°, aqueous EtOH; 3, XII, PhNCS, Et2O, 1-phenyl-3-(4-benzyl-1-piperazyl)thiourea, m. 180.5-82.0°, Me2CO-EtOH; 1, 1-(4-chlorophenyl)-4-aminopiperazine (XIII), III, EtOH, Et N-4-(4-chlorophenyl)-1-piperazylcarbamate, m. 194.5-5.5°, Me2CO; 2, XIII, Ac2O, AcOH, 1-(4-chlorophenyl)-4-acetyl-aminopiperazine, m. 211.5-13.0°, EtOH; 3, XIII, IV, Et2O, 1-phenyl-3-[4-(4-chlorophenyl)piperazyl] urea, m. 230.5-31.0°, PhCl; 3, XIII, o-ClC6H4NCS, Et2O, 1-(2-chlorophenyl)-3-[4-(4-chlorophenyl)-1-piperazyl]urea, m. 238.5-39.0°, CHCl3; 3, XIII, Et2NCOCl, Et2O, 1,1-diethyl-3-[4-(4-chlorophenyl)-1-piperazyl]urea, m. 108.5-9.0°, hexane; 3, XIII, VIII, Et2O, 1-allyl-3-[4-(4-chlorophenyl)-1-piperazyl]-thiourea, m. 198.5-200.0°, EtOH; 1, 1-(2-pyridyl)-4-aminopiperazine (XIV), III, EtOH, Et N-[4-(2-pyridyl)-1-piperazyl]carbamate, m. 133-4°, Et2O; 2, XIV, Ac2O, AcOH, 1-(2-pyridyl)-4-acetamidopiperazine, m. 172.5-3.5°, Me2CO; 3, XIV, IV, Et2O, 1-phenyl-3-[4-(2-pyridyl)-1-piperazyl]urea, m. 179.0-80.0°, Me2CO; 3, XIV, VIII, Et2O, 1-allyl-3-[4-(2-pyridyl)-1-piperazyl]thiourea, m. 155-6°, EtOH; 4, XIV, X, 10% aqueous NaOH, N-[4-(2-pyridyl)-1-piperazyl]-4-chlorobenzenesulfonamide, m. 173-4.5° (decompose), EtOH; 1, 1-(2-pyrimidyl)4-aminopiperazine (XV), III, EtOH, Et N-[4-(2-pyrimidyl)-1-piperazyl]carbamate, m. 186.5-7.5°, EtOH; 2, XV, Ac2O, AcOH, 1-(2-pyrimidyl)-4-acetamidopiperazine, m. 248.0-9.5°, EtOH; 3, XV, VII, Et2O, 1-cyclohexyl-3-[4-(2-pyrimidyl)-1-piperazyl]urea, m. 200.5-1.5°, Me2CO; 3, XV, IX, Et2O, 1-ethyl-3-[4-(2-pyrimidyl)-1-piperazyl]thiourea, m. 206.5-8.0°, EtOH.

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MISSING OPERATOR L7 IBIB
The search profile that was entered contains terms or
nested terms that are not separated by a logical operator.

=> d 1-7 l7 ibib abs hitstr

L7   ANSWER 1 OF 7  CAPLUS  COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER:         2004:326428  CAPLUS
DOCUMENT NUMBER:          140:357373
TITLE:                    Purification piperazine derivatives
INVENTOR(S):              Morimoto, Masao; Sato, Haruyo
PATENT ASSIGNEE(S):       Toray Fine Chemical K. K., Japan
SOURCE:                   Jpn. Kokai Tokkyo Koho, 22 pp.
                          CODEN: JKXXAF
DOCUMENT TYPE:            Patent
LANGUAGE:                 Japanese
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.          KIND   DATE        APPLICATION NO.        DATE
     ---------------     ----   --------    --------------------   --------
     JP 2004123629        A     20040422    JP 2002-291344         20021003
PRIORITY APPLN. INFO.:                      JP 2002-291344         20021003
OTHER SOURCE(S):          MARPAT 140:357373
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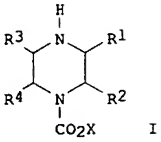
GI



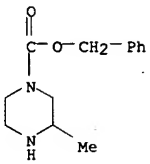
I

AB Piperaine derivs. I (R1, R2, R3, R4 = H, alkyl, alkoxy, halo, carboxyl, carbamoyl, alkylcarbamoyl; X = alkyl, alkenyl, alkynylaralkyl, alkoxyaryl; except R1-R4 = H) were purified by dissolved the crude compds. in water at pH ≤ 3 at 20° and washed with organic solvent having <10 wt% mutual solubility, or by distillation Thus, 2-methylpiperazine was treated with benzyl chlorocarbonate in BuOH at 0° for 2 h, and BuOH was remover by distillation, water and 35% HCl was added to adjusted pH to 0.8, washed with toluene several times to give, after treatment with 48% aqueous NaOH to pH 11.5, 1-benzyloxycarbonyl-3-methylpiperazine.

IT 84477-85-0P, 1-Benzyloxycarbonyl-3-methylpiperazine
612493-87-5P
RL: IMF (Industrial manufacture); PUR (Purification or recovery); SPN (Synthetic preparation); PREP (Preparation)
(purification piperazine derivs.)

RN 84477-85-0 CAPLUS

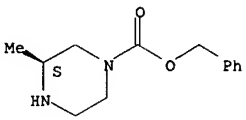
CN 1-Piperazinecarboxylic acid, 3-methyl-, phenylmethyl ester (9CI) (CA INDEX NAME)



RN 612493-87-5 CAPLUS

CN 1-Piperazinecarboxylic acid, 3-methyl-, phenylmethyl ester, (3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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L7   ANSWER 2 OF 7  CAPLUS  COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER:         2004:220323  CAPLUS
DOCUMENT NUMBER:          140:253580
```

TITLE: Process for producing oxycarbonyl -substituted piperazine derivative

INVENTOR(S): Morimoto, Masao; Sato, Haruyo

PATENT ASSIGNEE(S): Toray Fine Chemicals Co,. Ltd., Japan

SOURCE: PCT Int. Appl., 54 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

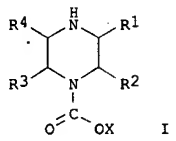
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004022548	A1	20040318	WO 2003-JP11204	20030902
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2003264365	A1	20040329	AU 2003-264365	20030902
EP 1548010	A1	20050629	EP 2003-794183	20030902
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
CN 1681797	A	20051012	CN 2003-821231	20030902
JP 2004115510	A	20040415	JP 2003-314809	20030905
US 2006161003	A1	20060720	US 2005-524517	20050211
PRIORITY APPLN. INFO.:			JP 2002-260376 A	20020905
			WO 2003-JP11204 W	20030902

OTHER SOURCE(S): CASREACT 140:253580; MARPAT 140:253580

GI



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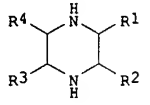


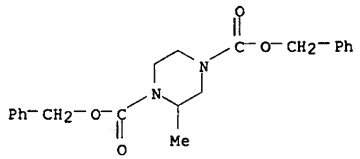
II

AB Disclosed is a process for producing an oxycarbonyl-substituted piperazine derivative [I; R1-R4 = H, C1-4 alkyl, C1-4 alkoxy, halo, CO2H, CONH2, C1-4 alkylcarbamoyl; X = C1-4 alkyl, C2-4 alkenyl, C2-4 alkynyl, (un)substituted aralkyl or aryl; wherein a compound represented by R1-R4 = H is excluded] from a piperazine derivative (II; R1-R4 = same as above), wherein the piperazine derivative is oxycarbonylated by the use of an organic solvent whose water content is 15% or less. Thus; 2-methylpiperazine (5.00 g, 0.0499 mol)was dissolved in 44 g 1-butanol (0.05 weight% H2O content), cooled to 0°, treated dropwise with 10.1 g g benzyl chloroformate (0.0579 mol, 1.17 equiv)at 0-8°, and stirred at 0-5° for 2 h and at room temperature for 12 h to give 95.1% 1-benzyloxycarbonyl-3-methylpiperazine.

IT 671198-52-0P, 1,4-Bis(benzyloxycarbonyl)-2-methylpiperazine
RL: BYP (Byproduct); PREP (Preparation)
(process for producing oxycarbonyl-substituted piperazine derivs. by oxycarbonylation of piperazine derivative in organic solvent with water content of ≤15%)

RN 671198-52-0 CAPLUS

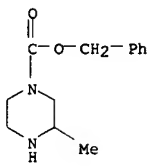
CN 1,4-Piperazinedicarboxylic acid, 2-methyl-, bis(phenylmethyl) ester (9CI) (CA INDEX NAME)



IT 84477-85-0P, 1-Benzyloxycarbonyl-3-methylpiperazine
120737-59-9P, 1-tert-Butoxycarbonyl-3-methylpiperazine
612493-87-5P, (S)-1-Benzyloxycarbonyl-3-methylpiperazine
RL: SPN (Synthetic preparation); PREP (Preparation)
(process for producing oxycarbonyl-substituted piperazine derivs. by oxycarbonylation of piperazine derivative in organic solvent with water content of ≤15%)

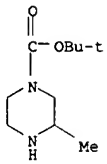
RN 84477-85-0 CAPLUS

CN 1-Piperazinecarboxylic acid, 3-methyl-, phenylmethyl ester (9CI) (CA INDEX NAME)



RN 120737-59-9 CAPLUS

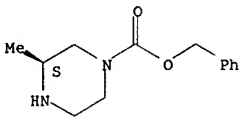
CN 1-Piperazinecarboxylic acid, 3-methyl-, 1,1-dimethylethyl ester (CA INDEX NAME)



RN 612493-87-5 CAPLUS

CN 1-Piperazinecarboxylic acid, 3-methyl-, phenylmethyl ester, (3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 3 OF 7 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:58066 CAPLUS
DOCUMENT NUMBER: 138:112415
TITLE: Preparation of amide-containing oxazolidinones having improved solubility and bioavailability
INVENTOR(S): Hester, Jackson B., Jr.
PATENT ASSIGNEE(S): Pharmacia & Upjohn Company, USA
SOURCE: PCT Int. Appl., 331 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003006440	A2	20030123	WO 2002-US22526	20020712
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2452513	A1	20030123	CA 2002-2452513	20020712
AU 2002354579	A1	20030129	AU 2002-354579	20020712
US 2004014967	A1	20040122	US 2002-194914	20020712
US 7049443	B2	20060523		
EP 1451164	A2	20040901	EP 2002-752358	20020712
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE				
JP 2005520782	T	20050714	JP 2003-512212	20020712
MX 2004PA00357	A	20040504	MX 2004-PA357	20040112
PRIORITY APPLN. INFO.:			US 2001-304808P P	20010712
			WO 2002-US22526 W	20020712

OTHER SOURCE(S): MARPAT 138:112415
GI

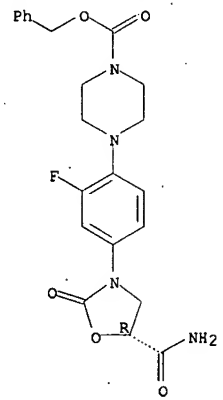
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The present invention is directed to amide-containing oxazolidinones (1) which have an improved solubility (no data) and a method of improving the solubility of amide-containing oxazolidinone bactericides. A very broad range of compds. 1 is claimed (see claims for details). Also claimed is a method of conversion of amide-containing oxazolidinones to more water-soluble derivs. comprising reaction with 3-(2-((dipropoxyphosphinyl)oxy)-4,6-dimethylphenyl)-3-methylbutanoyl chloride to form a C(O)NRC(O) or C(O)NRC(S) linkage followed by deprotection to give a phosphoric acid monoester. However, the only example is somewhat different in that I is prepared starting from II and III, followed by N-acylation and hydrogenation. In addition to the presence of the phosphonooxy group in compds. 1, also claimed are compds. 1 containing an acyloxy group. The bioavailability of these oxazolidinones is improved by improving the solubility thereof. Also included in the examples are prepns. of .apprx.25 amide-containing oxazolidinones, from which compds. 1 can potentially be prepared

IT 487041-21-4P, (-)-Phenylmethyl 4-[4-[(5R)-5-(aminocarbonyl)-2-oxooxazolidin-3-yl]-2-fluorophenyl]-1-piperazinecarboxylate
487041-22-5P, 1-(Phenylmethyl) 4-[4-((5R)-5-carboxy-2-oxooxazolidin-3-yl)-2-fluorophenyl]-1-piperazinecarboxylate
487041-23-6P, Phenylmethyl 4-[2-fluoro-4-[(5R)-5-(methoxycarbonyl)-2-oxooxazolidin-3-yl]phenyl]-1-piperazinecarboxylate
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation for potential conversion to more water-soluble and bioavailable derivs. containing acyloxy or phosphonooxy functionality)

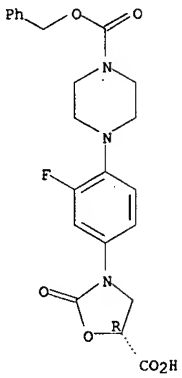
RN 487041-21-4 CAPLUS
CN 1-Piperazinecarboxylic acid, 4-[4-[(5R)-5-(aminocarbonyl)-2-oxo-3-oxazolidinyl]-2-fluorophenyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



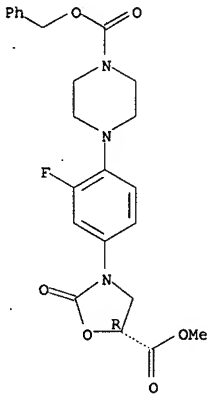
RN 487041-22-5 CAPLUS
CN 1-Piperazinecarboxylic acid, 4-[4-[(5R)-5-carboxy-2-oxo-3-oxazolidinyl]-2-fluorophenyl]-, 1-(phenylmethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 487041-23-6 CAPLUS
CN 1-Piperazinecarboxylic acid, 4-[2-fluoro-4-[(5R)-5-(methoxycarbonyl)-2-oxo-3-oxazolidinyl]phenyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



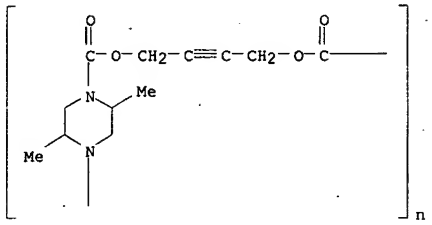
L7 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1968:78768 CAPLUS
DOCUMENT NUMBER: 68:78768
TITLE: Acetylenically unsaturated polyesters, polycarbonates, and polyurethanes
PATENT ASSIGNEE(S): Union Carbide Corp.
SOURCE: Brit., 16 pp.
CODEN: BRXXAA
DOCUMENT TYPE: Patent
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
GB 1103305		19680214	GB 1965-5839	19650210
US 3380965		19680430	US 1964-343453	19640210
US 3484411		19691216	US	19670410

PRIORITY APPLN. INFO.: US 19640210
GI For diagram(s), see printed CA Issue.
AB The synthesis of acetylenically unsatd. polyesters, polycarbonates, and polyurethanes having very useful phys. properties and heat stability at ≤300° is described. The polyesters are prepared by condensation of an acetylenic diol with a diacyl halide at 30-180° in an aromatic or chlorinated aliphatic hydrocarbon solvent, the polycarbonates are obtained by the base-catalyzed interfacial polycondensation of an acetylenic diol with a dihaloformate at -10 to +50° in an aromatic or chlorinated aliphatic hydrocarbon, and the polyurethanes are prepared by the interfacial condensation of an acetylenic glycol dihaloformate with a secondary amine. Thus, 0.86 g. 2-butyne-1,4-diol (I), 2.03 g. isophthaloyl chloride, and 15 ml. sym-tetrachloroethane was refluxed 27 hrs. under argon, the viscous residue dissolved in 50 ml. CHCl3, and the solution filtered through Celite and added to 500 ml. iso-PrOH to give a 75% yield of white, fibrous polyester having a reduced sp. viscosity of 0.75 at 25° and forming a film having a glass-transition temperature of 50°, m.p. 100°, tensile modulus 35,000 psi., tensile strength 3200 psi., and crystallinity 30%. Similarly prepared was a 1,4-cis-cyclohexanedicarboxylic acid-I polyester and a terephthalic acid-3-hexyne-2,5-diol polyester. N,N-Dimethylaniline (48.4 g.) in 100 ml. CH2Cl2 was added during 21 min. at 5-13° to 17.2 g. I, 300 ml. CH2Cl2, and 30.7 ml. liquid COCl2, the mixture stirred 30 min. and devolatilized under vacuum at 30-5°, the residue extracted with 400 ml. Et2O, the organic extract filtered through Celite and evaporated, and the residue dissolved in C6H6 and filtered through magnesia-silica to give 2-butyne-1,4-diol dichloroformate (II), b0.4-0.6 85-92°, nD25 1.4770. II (2.11 g.) in 30 ml. CH2Cl2 was added during 12 min. to 3.24 g. α-bisphenol (III), 1 g. NaOH, 50 ml. H2O, 5 drops Et3N, and 30 ml. CH2Cl2, the mixture stirred for 20 min. with the addition of 5 more drops Et3N, the organic layer washed with H2O and then with 400 ml. H2O containing 3 ml. concentrated H3PO4, the aqueous layer of pH 1.4 washed with water until pH 5-7, and the organic layer added to 600 ml. iso-PrOH to give an 80% yield of white, fibrous polycarbonate having a reduced sp. viscosity of 0.99 at 25°. Similarly prepared were bisphenol A-bisphenol A dichloroformate-II polycarbonate, polycarbonates from II and bisphenol A, 1,3-bis(p-hydroxyphenyl)-1-ethylcyclohexane, α-bisphenol, 2,2-bis(2,3,4,6-tetrachloro-4-hydroxyphenyl)propane, acetophenone bisphenol, 2,2-bis(2,6-dichloro-4-hydroxyphenyl)propane, cyclohexanone bisphenol, bis(4-hydroxyphenyl) sulfone, bisphenol of 1,4-dimethylenecyclohexane, bisphenol of α,α'-dichloro-p-xylene, bisphenol bis(chloromethyl)durene, β-bisphenol (IV)-γ-bisphenol (V), and bisphenol A-1,4-diphenol-2-butyne-1,4-diol dichloroformate polycarbonate. Treatment of 1.14 g. trans-2,5-dimethylpiperazine (VI), 15 ml. H2O, 1 g. NaOH, 3 drops Et3N, and 20 ml. CH2Cl2 with 2.11 g. II in 20 ml. CH2Cl2 gave a 96.8% yield of a polyurethane having a softening point of 75° and a reduced viscosity of 0.28. Similarly prepared were poly(carbonate urethanes) from II, VI, and bisphenol A, β-bisphenol-γ-bisphenol, or 1,3-bis(p-hydroxyphenyl)-1-ethylcyclohexane.
IT 32030-58-3P
RL: IMF (Industrial manufacture); PRP (Properties); PREP (Preparation)
(manufacture and properties of)
RN 32030-58-3 CAPLUS

CN Poly[(trans-2,5-dimethyl-1,4-piperazinediyl)carbonyloxy-2-butyne-1,4-diyloxycarbonyl] (9CI) (CA INDEX NAME)

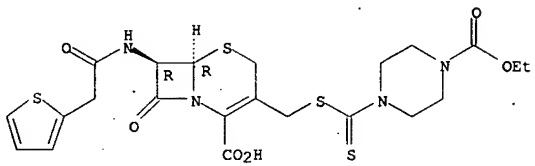


L7 ANSWER 5 OF 7 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1966:104252 CAPLUS
DOCUMENT NUMBER: 64:104252
ORIGINAL REFERENCE NO.: 64:19625a-f
TITLE: Dithiocarboxylated cephalosporins
INVENTOR(S): Heyningen, Earle Van; Brown, Carter N.
PATENT ASSIGNEE(S): Eli Lilly & Co.
SOURCE: 5 pp.
DOCUMENT TYPE: Patent
LANGUAGE: Unavailable
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 3239516		19660308	US 1965-426392	19650118
NL 6600248			NL	
PRIORITY APPLN. INFO.:			US	19650118

GI For diagram(s), see printed CA Issue.
AB The preparation is described of the title compds. (I) and betaines (II), which show resistance to the destructive action of penicillinase and have a high degree of activity against a broad range of both gram-pos. and gram-neg. pathogens. Thus, 0.0012 mole Na 7-acylamidocephalosporanate and an equimolar amount of Na piperazinodithiocarboxylate (III) were dissolved in 10 ml. H2O, the mixture heated at 40-5° for 24 hrs., and filtered. From the filtrate was precipitated a yellow glass by addition of an equal volume of aqueous saturated NaCl solution and chilling for several hrs. The supernatent solution was decanted and the solid dissolved in 25-50 ml. CHCl3. The CHCl3 solution was washed with 50% saturated aqueous NaCl solution, evaporated to half its volume, diluted with Et2O and chilled to give I. The I (R1 = α-thienyl) prepared were (R2 and % yield given): Me, 23.5; Et, 6.1; Pr, 25.2; iso-Pr, 13.3; Bu, 23.2; amyl, 14.2; β-hydroxyethyl, 9.6. Other I prepared were α-thienylmethyl 2- carboxy-4-methylpiperazinodithiocarboxyl ate cephalosporin and phenylthiomethyl 4-methylpiperazinodithiocarboxylate cephalosporin. II were prepared by mixing a solution of 0.01 mole of the crude Na salt of I in 100 ml. dry CHCl3 with a solution of 0.0105 mole alkyl or alkenyl halide in 10 ml. CHCl3. The mixture was held at room temperature with occasional shaking for 4-7 days during which time a solid precipitated The precipitate was separated, air-dried, and triturated with water. The product was dissolved in HCON-Me2 (25-35 ml./g.) by warming gently and adding H2O until the cloudiness cleared. Tetrahydrofuran (5-10 vols.) was added, and the turbid mixture cooled to give II. The following II (R1 = α-thienyl, R2 = Me) were prepared (R3 and % yield given): Me, 48; Pr, 26.4; allyl 66.3; Bu, 25. The following III were also prepared in which the substituent at the 4 position of the piperazine ring is referred to as R2 (R2, m.p., and % yield given): Me, >290°, 45.5; Et, 232-5°, 76; Pr, 265-8°, 80; iso-Pr, 262-6°, 61.7; Bu, 248-50°, 63; amyl, 254-8°, 85. The uv spectra of I and II were recorded.
IT 5712-83-4P, 1,4-Piperazinedicarboxylic acid, 1,1-dithio-, 4-ethyl ester, S-ester with 3-(mercaptomethyl)-8-oxo-7-[2-(2-thienyl)acetamido]-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid, Na salt
5712-84-5P, 1,4-Piperazinedicarboxylic acid, 1,1-dithio-, 4-ethyl ester, S-ester with 3-(mercaptomethyl)-8-oxo-7-[2-(2-thienyl)acetamido]-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid
RL: PREP (Preparation)
(preparation of)
RN 5712-83-4 CAPLUS
CN 1,4-Piperazinedicarboxylic acid, 1,1-dithio-, 4-ethyl ester, ester with 3-(mercaptomethyl)-8-oxo-7-[2-(2-thienyl)acetamido]-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid monosodium salt (8CI) (CA INDEX NAME)

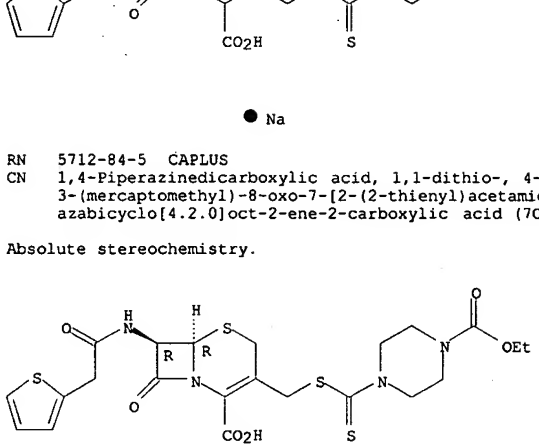
Absolute stereochemistry.



● Na

RN 5712-84-5 CAPLUS
CN 1,4-Piperazinedicarboxylic acid, 1,1-dithio-, 4-ethyl ester, S-ester with 3-(mercaptomethyl)-8-oxo-7-[2-(2-thienyl)acetamido]-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid (7CI, 8CI) (CA INDEX NAME)

Absolute stereochemistry.



L7 ANSWER 6 OF 7 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1965:59429 CAPLUS
DOCUMENT NUMBER: 62:59429
ORIGINAL REFERENCE NO.: 62:10562c-e
TITLE: Monoazo dyes
INVENTOR(S): Wunderlich, Hermann; Wolfrum, Gerhard
PATENT ASSIGNEE(S): Farbenfabriken Bayer A.-G.
SOURCE: 16 pp.

DOCUMENT TYPE: Patent
LANGUAGE: Unavailable
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
BE 638210		19640203	BE	
PRIORITY APPLN. INFO.:			DE	19621005

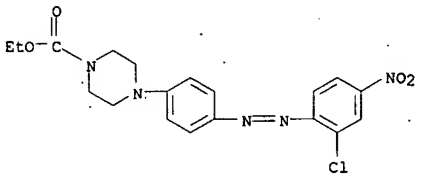
GI For diagram(s), see printed CA Issue.

AB Dyes which are insol., or difficultly soluble, in water for dyeing and printing synthetic fibers, especially polyesters and cellulose esters, with the aid of dispersants, have the general formula I and are prepared by coupling a diazonium salt with a 1-acyl-4-phenylpiperazine derivative Thus, 2,4-Cl(O2N)C6H3NH2 (II) 2.7 was diazotized and coupled in AcOH 10 with N-methyl-4-(m-tolyl)-1-piperazinecarboxamide (III) 4.9 parts, m. 99° (from molar amts. of MeNCO and 1-(m-tolyl)piperazine (IV) in CH2Cl2 or C6H6 at 10° with slight heating in the absence of moisture) to give I (X = O2N, Y = Cl, Z = Me, R = CONHMe), a bluish red dye. Other I were similarly prepared (X, Y, Z, R, and shade given): O2N, H, Cl, Ac, orange; O2N, Cl, H, COC6H4OH-2, yellowish-red; Cl, O2N, H, COC6H3Cl2-2,4, yellowish red; O2N, Cl, H, CO2Et, yellowish red; O2N, Cl, H, COCH2Ac, red; O2N, CN, H, COCH2CH2Cl, bluish red; Cl, Cl, H, SO2Me, reddish yellow. Also prepared was 5-amino-3-phenyl-1,2,4-thiadiazole → N-dimethyl analog of III, red. Prepns. of the following 1-acylpiperazines are reported (acyl group and m.p. given): CONMe2, --; Ac, --; COC6H4OH-2, 163-4°; COC6H3Cl2-2,4, --; CO2Et, --; SO2Me, --; COCH2Ac, 50-1°; COCH2CH2Cl, 87-8°.

IT 3960-34-7P, 1-Piperazinecarboxylic acid, 4-[p-[(2-chloro-4-nitrophenyl)azo]phenyl]-, ethyl ester
RL: PREP (Preparation)
(preparation of)

RN 3960-34-7 CAPLUS

CN 1-Piperazinecarboxylic acid, 4-[p-[(2-chloro-4-nitrophenyl)azo]phenyl]-, ethyl ester (7CI, 8CI) (CA INDEX NAME)



L7 ANSWER 7 OF 7 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1955:24199 CAPLUS
DOCUMENT NUMBER: 49:24199
ORIGINAL REFERENCE NO.: 49:4730i,4731a-i,4732a
TITLE: Amino piperazines
INVENTOR(S): Conroy, Edward A.; Parker, Robert P.
PATENT ASSIGNEE(S): American Cyanamid Co.
DOCUMENT TYPE: Patent
LANGUAGE: Unavailable
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2663707		19531222	US 1951-233126	19510622

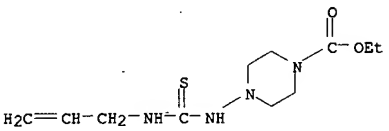
GI For diagram(s), see printed CA Issue.

AB Substituted N-aminopiperazines having central nervous system depressant, anticonvulsant, sedative, anesthetic or analgesic action are prepared RN.CHY1.CH2.NNHZ.CHY2.CH2 (I), where Z=H, Y1 and Y2 = Me or H, R = alkyl, aralkyl, monocyclic aryl, carbalkoxy, di-alkylcarbamyl, or heterocyclic radical. In the product, Z is a carbalkoxy, carbamoyl, thiocarbamoyl, or acyl radical. Method 1. 1-Carbethoxy-4-aminopiperazine (II) 35 and NaHCO3 21 parts in absolute EtOH 80 parts stirred below 50° while a solution of EtO2CCl (III) 21.5 in absolute EtOH 80 parts is added, the mixture refluxed 2 h., filtered, and the EtOH evaporated give Et N-(4-carbethoxy-1-piperazyl)carbamate, m. 143.5-4.5° (from Et2O). Method 2. II 34.6, Ac2O 20.5, and AcOH 150 parts heated (water bath) for 30 min., then poured into water 500 and concentrated ammonia 180 parts, the solution extracted with CHCl3 and the CHCl3 evaporated gives 1-carbethoxy-4-acetamidopiperazine, m. 180.5-1.0° (from acetone). Method 3. Ph isocyanate (IV) 75 in Et2O 75 parts added to II 26 in Et2O 150 parts over 10 min. at ice-bath temperature and the mixture filtered gives 1-phenyl-3-(4-carbethoxy-1-piperazyl)urea, m. 143.5-4.5° (from Me2CO-hexane). Method 4. Benzoyl chloride 28.1 added (10 min.) to a solution of 1-diethylcarbamoyl-4-aminopiperazine (V) 37 in 5% aqueous NaOH 150 parts, the mixture extracted with CHCl3, the CHCl3 evaporated gives 1-diethylcarbamoyl-4-benzoylaminopiperazine, m. 111-12° (from Me2CO-Et2O). The following list of products was also prepared The method number, starting material, other reactant, solvent, product, m. or b.p. of product, and crystallization solvent are given. 1, II, PhCH2COCl (VI), benzene, 1-carbethoxy-4-phenylacetyl-aminopiperazine, m. 138-9°, EtOAc; 3, II, cyclohexyl isocyanate (VII), Et2O, 1-cyclohexyl-3-(4-carbethoxy-1-piperazyl)urea, m. 159.5-60.5°, Me2CO-hexane; 3, II, PhNCS, Et2O, 1-phenyl-3-(4-carbethoxy-1-piperazyl)thiourea, m. 189-90°, EtOH; 3, II, allyl isothiocyanate (VIII), Et2O, 1-allyl-3-(4-carbethoxy-1-piperazyl)thiourea, m. 132-3°, Me2CO-hexane; 1, V, III, EtOH, Et N-(4-diethylcarbamoyl-1-piperazyl)carbamate, b5.0 200-5°, -; 2, V, Ac2O, AcOH, 1-diethylcarbamoyl-4-acetylaminopiperazine, m. 85.5-6.5°, Me2CO-Et2O; 3, V, IV, Et2O, 1-phenyl-3-(4-diethylcarbamyl-1-piperazyl)urea, m. 111-13°, Me2CO-hexane; 3, V, VII, Et2O, 1-cyclohexyl-3-(4-diethylcarbamoyl-1-piperazyl)urea, m. 98.0-9.5°, hexane; 3, V, EtNCS (IX), Et2O, 1-ethyl-3-(4-diethylcarbamoyl-1-piperazyl)thiourea, m. 146-7°, Me2CO-hexane; 4, V, 4-chlorobenzenesulfonyl chloride (X), 5% NaOH, N-(4-diethylcarbamoyl-1-piperazyl)-4-chlorobenzenesulfonamide, m. 150.5-1.5°, aqueous EtOH; 1, 1-methyl-4-aminopiperazine (XI), III, EtOH, Et N-(4-methyl-4-aminopiperazyl)carbamate, b3 122-4°; 3, XI, VII, Et2O, 1-cyclohexyl-3-(4-methyl-1-piperazyl)urea, m. 159.5-60.0°, Me2CO; 3, XI, IX, Et2O, 1-ethyl-3-(4-methyl-1-piperazyl)thiourea, m. 156.2-6.7°, Me2CO; 1, 1-benzyl-4-aminopiperazine (XII), III, EtOH, Et N-(4-benzyl-1-piperazyl)carbamate, m. 95.5-6.5°, hexane; 2, XII, Ac2O, AcOH, 1-benzyl-4-acetamidopiperazine, m. 136-7°, Me2CO; 4, XII, VI, benzene-pyridine, 1-benzyl-4-phenylacetamidopiperazine, m. 161.0-1.7°, Me2CO; 4, XII, BzCl, 5% NaOH, 1-benzyl-4-benzoylaminopiperazine, m. 173-4°, Me2CO; 3, XII, IV, Et2O, 1-phenyl-3-(4-benzyl-1-piperazyl)urea, m. 135.0-5.5°, aqueous EtOH; 3, XII, PhNCS, Et2O, 1-phenyl-3-(4-benzyl-1-piperazyl)thiourea, m. 180.5-82.0°, Me2CO-EtOH; 1, 1-(4-chlorophenyl)-4-aminopiperazine (XIII), III, EtOH, Et N-4-(4-chlorophenyl)-1-piperazylcarbamate, m. 194.5-5.5°, Me2CO; 2, XIII, Ac2O, AcOH, 1-(4-chlorophenyl)-4-acetyl-aminopiperazine, m. 211.5-13.0°, EtOH; 3, XIII, IV, Et2O, 1-phenyl-3-[4-(4-chlorophenyl)piperazyl] urea, m. 230.5-31.0°, PhCl; 3, XIII, o-ClC6H4NCS, Et2O, 1-(2-chlorophenyl)-3-[4-(4-chlorophenyl)-1-piperazyl]urea, m. 238.5-39.0°, CHCl3; 3, XIII, Et2NCOCl, Et2O, 1,1-diethyl-3-[4-(4-chlorophenyl)-1-piperazyl]urea, m. 108.5-9.0°, hexane; 3, XIII, VIII, Et2O, 1-allyl-3-[4-(4-chlorophenyl)-1-piperazyl]-thiourea, m. 198.5-200.0°, EtOH; 1, 1-(2-pyridyl)-4-aminopiperazine (XIV), III, EtOH, Et N-[4-(2-pyridyl)-1-piperazyl]carbamate, m.

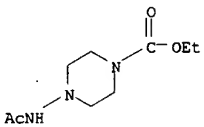
133-4°, Et2O; 2, XIV, Ac2O, AcOH, 1-(2-pyridyl)-4-acetamidopiperazine, m. 172.5-3.5°, Me2CO; 3, XIV, IV, Et2O, 1-phenyl-3-[4-(2-pyridyl)-1-piperazyl]urea, m. 179.0-80.0°, Me2CO; 3, XIV, VIII, Et2O, 1-allyl-3-[4-(2-pyridyl)-1-piperazyl]thiourea, m. 155-6°, EtOH; 4, XIV, X, 10% aqueous NaOH, N-[4-(2-pyridyl)-1-piperazyl]-4-chlorobenzenesulfonamide, m. 173-4.5° (decompose), EtOH; 1, 1-(2-pyrimidyl)4-aminopiperazine (XV), III, EtOH, Et N-[4-(2-pyrimidyl)-1-piperazyl]carbamate, m. 186.5-7.5°, EtOH; 2, XV, Ac2O, AcOH, 1-(2-pyrimidyl)-4-acetamidopiperazine, m. 248.0-9.5°, EtOH; 3, XV, VII, Et2O, 1-cyclohexyl-3-[4-(2-pyrimidyl)-1-piperazyl]urea, m. 200.5-1.5°, Me2CO; 3, XV, IX, Et2O, 1-ethyl-3-[4-(2-pyrimidyl)-1-piperazyl]thiourea, m. 206.5-8.0°, EtOH.

IT 872829-26-0P, 1-Piperazinecarboxylic acid, 4-(3-allyl-2-thioureido)-, ethyl ester 872829-27-1P, 1-Piperazinecarboxylic acid, 4-acetamido-, ethyl ester 872829-47-5P, 1-Piperazinecarboxylic acid, 4-(3-phenylureido)-, ethyl ester 872829-48-6P, 1-Piperazinecarboxylic acid, 4-(3-phenyl-2-thioureido)-, ethyl ester 872829-50-0P, 1-Piperazinecarboxylic acid, 4-(2-phenylacetamido)-, ethyl ester 872829-57-7P, 1-Piperazinecarboxylic acid, 4-(3-cyclohexylureido)-, ethyl ester 875229-22-4P, 1-Piperazinecarbamic acid, 4-carboxy-, diethyl ester
RL: PREP (Preparation)
(preparation of)

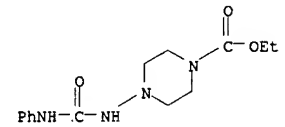
RN 872829-26-0 CAPLUS
CN 1-Piperazinecarboxylic acid, 4-(3-allyl-2-thioureido)-, ethyl ester (5CI) (CA INDEX NAME)



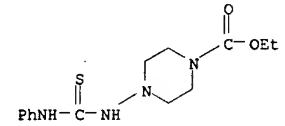
RN 872829-27-1 CAPLUS
CN 1-Piperazinecarboxylic acid, 4-acetamido-, ethyl ester (5CI) (CA INDEX NAME)



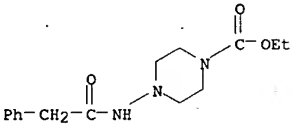
RN 872829-47-5 CAPLUS
CN 1-Piperazinecarboxylic acid, 4-(3-phenylureido)-, ethyl ester (5CI) (CA INDEX NAME)



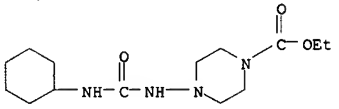
RN 872829-48-6 CAPLUS
CN 1-Piperazinecarboxylic acid, 4-(3-phenyl-2-thioureido)-, ethyl ester (5CI) (CA INDEX NAME)



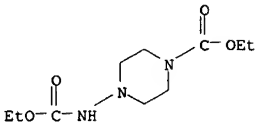
RN 872829-50-0 CAPLUS
CN 1-Piperazinecarboxylic acid, 4-(2-phenylacetamido)-, ethyl ester (5CI) (CA INDEX NAME)



RN 872829-57-7 CAPLUS
CN 1-Piperazinecarboxylic acid, 4-(3-cyclohexylureido)-, ethyl ester (5CI) (CA INDEX NAME)



RN 875229-22-4 CAPLUS
CN 1-Piperazinecarbamic acid, 4-carboxy-, diethyl ester (5CI) (CA INDEX NAME)



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         3814 PIPERAZINES
        30261 PIPERAZINE
                (PIPERAZINE OR PIPERAZINES)
L8          0 1-CARBOXY-PIPERAZINE
                (1(W)CARBOXY(W)PIPERAZINE)

=> s carbox? and piperazine
       607098 CARBOX?
        29395 PIPERAZINE
         3814 PIPERAZINES
        30261 PIPERAZINE
                (PIPERAZINE OR PIPERAZINES)
L9         4980 CARBOX? AND PIPERAZINE

=> s l9 and water
       2561153 WATER
        265715 WATERS
       2618195 WATER
                (WATER OR WATERS)
L10         389 L9 AND WATER

=> s l10 and solvent
        707350 SOLVENT
        342575 SOLVENTS
        884926 SOLVENT
                (SOLVENT OR SOLVENTS)
L11          87 L10 AND SOLVENT

=> s l11 and (method or process)
       3448306 METHOD
       1384711 METHODS
       4442866 METHOD
                (METHOD OR METHODS)
       2461917 PROCESS
       1673139 PROCESSES
       3669668 PROCESS
                (PROCESS OR PROCESSES)
L12          36 L11 AND (METHOD OR PROCESS)

=> d 1-36 ibib abs

L12  ANSWER 1 OF 36  CAPLUS  COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER:         2006:817610  CAPLUS
DOCUMENT NUMBER:          145:230652
TITLE:                    Preparation of a crystalline form of
                          5-[[(1S)-2-((2R)-4-benzoyl-2-methylpiperazin-1-yl)-1-
                          methyl-2-oxoethyl]oxy]-4-methoxypyridine-2-
                          carboxylic acid methylamide for the treatment
                          of HIV
INVENTOR(S):              Fenwick, David Roy; Gillmore, Adam Thomas; Platts,
                          Michelle Yvette
PATENT ASSIGNEE(S):       Pfizer Limited, UK
SOURCE:                   PCT Int. Appl., 47pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.          KIND   DATE        APPLICATION NO.        DATE
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     WO 2006085199        A1    20060817    WO 2006-IB255          20060203
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
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             GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR,
             KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX,
             MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE,
             SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC,
             VN, YU, ZA, ZM, ZW
         RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
             IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ,
             CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH,
             GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
             KG, KZ, MD, RU, TJ, TM
     JP 2006225388        A     20060831    JP 2006-34726          20060213
PRIORITY APPLN. INFO.:                      GB 2005-3043        A  20050214
                                            US 2005-662184P     P  20050315

OTHER SOURCE(S):          CASREACT 145:230652
AB   The present invention is related to a crystalline form of 5-[[(1S)-2-((2R)-4-
     Benzoyl-2-methylpiperazin-1-yl)-1-methyl-2-oxoethyl]oxy]-4-methoxypyridine-
     2-carboxylic acid methylamide (I), processes for the
     preparation thereof, compns. containing the crystalline form, and uses of the
crystalline
     form.  The invention is also related to the ability of I to inhibit the
     interaction of gp120 with CD4 and the use of the crystalline form and compns.
     thereof in the treatment of HIV, a retroviral infection genetically
     related to HIV, or AIDS.  Thus, coupling (S)-2-[(4-methoxy-6-
     methylcarbamoylpyridin-3-yl)oxy]propionic acid•HCl (preparation given) with
     (3R)-(3-methylpiperazin-1-yl)phenylmethanone (preparation given) in
     N,N-dimethylacetamide, and recrystn. from Bu acetate gave (-)-I, which
     showed a sharp endothermic melting peak around 127°.  In a gp160
     induced cell-cell fusion assay, I had an IC50 of 14 nM against HIV-1
     fusion.
REFERENCE COUNT:          2     THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS
                                RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12  ANSWER 2 OF 36  CAPLUS  COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER:         2005:823666  CAPLUS
DOCUMENT NUMBER:          143:229882
TITLE:                    Process for preparing purified ciprofloxacin
                          by contacting it with a solid support
INVENTOR(S):              Ruzic, Milos; Pucelj, Joze; Tomsic, Zdenka; Makuc,
                          Simon; Brne, Peter; Barut, Milos; Strancar, Ales
PATENT ASSIGNEE(S):       Krka, Tovarna Zdravil D.D. Novo Mesto, Slovenia
SOURCE:                   PCT Int. Appl., 25 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.          KIND   DATE        APPLICATION NO.        DATE
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     WO 2005075430        A1    20050818    WO 2005-EP975          20050201
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
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             GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
             LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
             NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
             TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
         RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
             AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
             EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT,
             RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML,
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MR, NE, SN, TD, TG

DE 102004005186	B3	20051013	DE 2004-102004005186	20040202
EP 1711468	A1	20061018	EP 2005-715236	20050201

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, BA, HR, IS, YU

PRIORITY APPLN. INFO.: DE 2004-102004005186A 20040202
WO 2005-EP975 W 20050201

AB A process for purifying of ciprofloxacin is described wherein a solution of ciprofloxacin, prepared in two steps by the condensation of N-(ethoxycarbonyl)piperazine with 7-chloro-1-cyclopropyl-6-fluoro-1,4-dihydro-4-oxoquinoline-3-carboxylic acid to give 1-cyclopropyl-7-[4-(ethoxycarbonyl)-1-piperazinyl]-6-fluoro-1,4-dihydro-4-oxoquinoline-3-carboxylic acid which was then hydrolyzed with aqueous KOH into ciprofloxacin, is contacted with a solid phase (e.g., Amberchrom CG-161S) such as is used in HPLC. An infusible dosage form of ciprofloxacin is presented.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 3 OF 36 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:730072 CAPLUS
DOCUMENT NUMBER: 143:376276
TITLE: Synthesis and Characterization of Water -Soluble Phenylene-Vinylene-Based Singlet Oxygen Sensitizers for Two-Photon Excitation
AUTHOR(S): Nielsen, Christian B.; Johnsen, Mette; Arnbjerg, Jacob; Pittelkow, Michael; McIlroy, Sean P.; Ogilby, Peter R.; Jorgensen, Mikkel
CORPORATE SOURCE: Polymer Department, Riso National Laboratory, Roskilde, DK-4000, Den.
SOURCE: Journal of Organic Chemistry (2005), 70(18), 7065-7079
CODEN: JOCEAH; ISSN: 0022-3263
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The synthesis and characterization of water-soluble singlet oxygen sensitizers with a phenylene-vinylene motif is presented. The principal motivation for this study was to better understand specific features of a water-soluble mol. that influence the photosensitized production of singlet oxygen upon nonlinear, two-photon excitation of that mol. To achieve water solubility, sensitizers were synthesized with ionic as well as nonionic substituents. In the ionic approach, salts of N-methylated pyridine, benzothiazole, and 1-methyl-piperazine moieties were used, as were aryl-substituted sulfonic acid moieties. In the nonionic approach, aryl-substituted triethylene glycol moieties were used. Selected photophys. properties of the compds. synthesized were determined, including singlet oxygen quantum yields. Of the mols. examined, the most efficient singlet oxygen sensitizers had triethylene glycol units as the functional group that imparted water solubility Mols. containing the ionic moieties did not make singlet oxygen in appreciable yield nor did they efficiently fluoresce. Rather, for these latter mols., rapid charge-transfer-mediated nonradiative processes appear to dominate excited state deactivation.

REFERENCE COUNT: 86 THERE ARE 86 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 4 OF 36 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:696872 CAPLUS
DOCUMENT NUMBER: 143:172650
TITLE: An efficient process for the manufacture of (E)-entacapone polymorphic form A
INVENTOR(S): Jaweed Mukarram, Siddiqui Mohammed; Khan, Rashid Abdul Rehman; Yavad, Ram Prasad
PATENT ASSIGNEE(S): Wockhardt Limited, India
SOURCE: PCT Int. Appl., 11 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005070881	A1	20050804	WO 2003-IB6176	20031224

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

AU 2003296838	A1	20050811	AU 2003-296838	20031224
EP 1701936	A1	20060920	EP 2003-819304	20031224

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, SK

US 2007004935	A1	20070104	US 2006-474732	20060626

PRIORITY APPLN. INFO.: WO 2003-IB6176 A 20031224
OTHER SOURCE(S): CASREACT 143:172650

AB (E)-N, N-Diethyl-2-cyano-3-(3,4-dihydroxy-5-nitrophenyl)acrylamide (Entacapone) polymorphic Form A, is prepared by the aldol condensation of 3,4-dihydroxy-5-nitrobenzaldehyde with N,N-diethylcyanoacetamide in presence of a base in an alc. solution After the disappearance of the reactants, the crude reaction mixture is poured into aqueous Et acetate solution followed by adjusting pH between 3.5-4.0 with acetic acid. A simple extraction process provides 99.7% HPLC pure (E)-isomer of Entacapone Form A.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 5 OF 36 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:638837 CAPLUS
DOCUMENT NUMBER: 143:133192
TITLE: Process for the preparation of stable polymorphic crystalline forms of entacapone
INVENTOR(S): Jaweed, Mukarram Siddiqui Mohammed; Khan, Rashid Abdul Rehman; Yadav, Ram Prasad; Shaikh, Zakir Gafoor
PATENT ASSIGNEE(S): Wockhardt Limited, India; Jaweed Mukarram, Siddiqui Mohammed
SOURCE: PCT Int. Appl., 24 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005066117	A1	20050721	WO 2003-IB6200	20031229

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RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ,

BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CA 2551791	A1	20050721	CA 2003-2551791		20031229
AU 2003292465	A1	20050812	AU 2003-292465		20031229
EP 1701937	A1	20060920	EP 2003-768046		20031229
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, SK					
BR 2003018690	A	20061226	BR 2003-18690		20031229
PRIORITY APPLN. INFO.:			WO 2003-IB6200	W	20031229

AB Stable crystalline polymorphic forms C and D of entacapone (I) and their preparation processes are described in which Form C is obtained by the Knoevenagel condensation of 3,4-dihydroxy-5-nitrobenzaldehyde and N,N-diethyl-2-cyanoacetamide in the presence of a base followed by addition of acetic acid after the reaction is over and a crystallization step. Form D is prepared from I Form C, Crystallog. pure Form A or crystallog. essentially pure From A. The polymorphic forms C and D of I are characterized by specific IR and X-ray powder diffraction peak values.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 6 OF 36 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:964359 CAPLUS
DOCUMENT NUMBER: 141:382955
TITLE: Reaction mixtures for preparation of inhibitor of hydrogen sulfide corrosion and hydrogenation of metals
INVENTOR(S): Lisitskii, V. V.; Gataullin, R. F.; Rasulev, Z. G.; Vakhitov, Kh. S.; Dmitriev, Yu. K.
PATENT ASSIGNEE(S): Zakrytoe Aktsionernoe Obshchestvo "Kaustik", Russia
SOURCE: Russ., No pp. given
CODEN: RUXXE7
DOCUMENT TYPE: Patent
LANGUAGE: Russian
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
RU 2239671	C1	20041110	RU 2003-106306	20030305
PRIORITY APPLN. INFO.:			RU 2003-106306	20030305

AB The corrosion inhibitors are prepared by: (a) reacting aliphatic monocarboxylic acids (especially α,α1-branched monocarboxylic acid) as C10-20 fraction with polyethylene-polyamines and 1,4-di(2-aminoethyl) piperazine at 250-280° for 2-6 h, using the acids:polyethylene-polyamines:piperazine derivative molar ratio of 1(0.7-0.9):(0.2-0.5); (b) distillation for removal of reaction water and excess polyethylene-polyamines for 2-4 h at 1-30 torr, and cooling the reactor to 160-180°. The resulting product is stirred with α,α1-branched monocarboxylic C10-20 acids (or tall-oil acids) charged at 1:1 molar ratio of the condensation product to acids, stirred for further 2-4 h, and cooled to 40-60°. The product is then mixed with 2-8% nonionic surfactant, 10-25% saturated monohydric C1-4 alc., and 32-73% blended aromatic solvent added with stirring to form homogeneous solution, and cooled. The resulting corrosion inhibitor has increased corrosion prevention efficiency, and promotes decreased hydrogenation (plasticity loss) of steel, and is suitable for use at nominally 25 mg/L in water-petroleum fluids.

L12 ANSWER 7 OF 36 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:703361 CAPLUS
DOCUMENT NUMBER: 141:174188
TITLE: An improved process for the preparation of ciprofloxacin
INVENTOR(S): Kalkote, Uttam Ramrao; Joshi, Rohini Ramesh; Joshi, Ramesh Anna; Deshpande, Vishnu Hari; Ravindranathan, Thottappillil
PATENT ASSIGNEE(S): Council of Scientific and Industrial Research, India
SOURCE: Indian, 10 pp.
CODEN: INXXAP
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
IN 184650	A1	20000923	IN 1996-DE1810	19960814
PRIORITY APPLN. INFO.:			IN 1996-DE1810	19960814
OTHER SOURCE(S):	CASREACT 141:174188			

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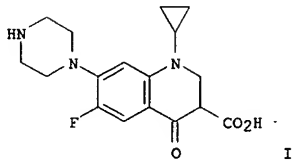

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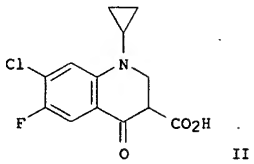

II

AB The invention is directed to an improved process for the preparation of ciprofloxacin (I) by amination of 1-cyclopropyl-7-chloro-6-fluoro-4-oxo-1,2,3,4-tetrahydroquinoline-3-carboxylic acid (II) with 1.5-2.5 equiv of piperazine at 120-200°C in a polar solvent such as water and ethanol or mixture thereof for 4 to 5 h, cooling the reaction mixture to room temperature and separating by conventional methods. The advantages include use of environmental friendly solvents, and of lower amts. of piperazine. Thus, heating 36 parts II with 27 parts piperazine in 100 parts EtOH at 140° for 5 h, filtering I from the reaction mixture, redissolving it in AcOH, filtering and neutralizing with NH4OH, and filtering again gave 63.7% I.

L12 ANSWER 8 OF 36 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:220323 CAPLUS
DOCUMENT NUMBER: 140:253580
TITLE: Process for producing oxycarbonyl-substituted piperazine derivative
INVENTOR(S): Morimoto, Masao; Sato, Haruyo
PATENT ASSIGNEE(S): Toray Fine Chemicals Co,. Ltd., Japan
SOURCE: PCT Int. Appl., 54 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004022548	A1	20040318	WO 2003-JP11204	20030902
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, KE, KG, KP, KR, KZ, LC, LK, LR, LS,				

LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG,
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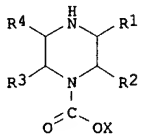
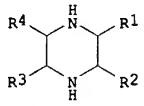
TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,
BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

AU 2003264365	A1	20040329	AU 2003-264365	20030902
EP 1548010	A1	20050629	EP 2003-794183	20030902
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
CN 1681797	A	20051012	CN 2003-821231	20030902
JP 2004115510	A	20040415	JP 2003-314809	20030905
US 2006161003	A1	20060720	US 2005-524517	20050211
PRIORITY APPLN. INFO.:			JP 2002-260376 A	20020905
			WO 2003-JP11204 W	20030902

OTHER SOURCE(S): CASREACT 140:253580; MARPAT 140:253580
GI


I


II

AB Disclosed is a process for producing an oxycarbonyl-substituted piperazine derivative [I; R1-R4 = H, C1-4 alkyl, C1-4 alkoxy, halo, CO2H, CONH2, C1-4 alkylcarbamoyl; X = C1-4 alkyl, C2-4 alkenyl, C2-4 alkynyl, (un)substituted aralkyl or aryl; wherein a compound represented by R1-R4 = H is excluded] from a piperazine derivative (II; R1-R4 = same as above), wherein the piperazine derivative is oxycarbonylated by the use of an organic solvent whose water content is 15% or less. Thus, 2-methylpiperazine (5.00 g, 0.0499 mol)was dissolved in 44 g 1-butanol (0.05 weight% H2O content), cooled to 0°, treated dropwise with 10.1 g g benzyl chloroformate (0.0579 mol, 1.17 equiv)at 0-8°, and stirred at 0-5° for 2 h and at room temperature for 12 h to give 95.1% 1-benzyloxycarbonyl-3-methylpiperazine.
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 9 OF 36 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:648272 CAPLUS
DOCUMENT NUMBER: 139:180088
TITLE: Process for the preparation of N-(2,3-dihydrobenzo[1,4]dioxin-2-carbonyl) piperazine via the amidation of piperazine with ethyl 2,3-dihydrobenzo[1,4]dioxin-2-carboxylate
INVENTOR(S): Pardhasaradhi, Malladi; Kumaraswamy, Gullapalli; Das Arun, Kanti; Nivedita, Jeena; Chembumkulam, Kamalakshyamma Snehalatha Nair; Sastry, Mudiganti Naga Venkata
PATENT ASSIGNEE(S): Council of Scientific & Industrial Research, India
SOURCE: U.S., 4 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6608200	B1	20030819	US 2002-266991	20021007
EP 1403263	A1	20040331	EP 2002-21686	20020927
EP 1403263	B1	20050622		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
PRIORITY APPLN. INFO.:			US 2002-266991 A	20021007

OTHER SOURCE(S): CASREACT 139:180088
AB An improved process for the preparation of N-(2,3-Dihydrobenzo[1,4]dioxin-2-carbonyl) piperazine includes heating a reaction mixture of Et 2,3-dihydrobenzo[1,4]dioxin-2-carboxylate and piperazine. The reaction mixture is then subjected to a series of aqueous sodium bicarbonate and washes and a chloroform extraction to yield N-(2,3-Dihydrobenzo[1,4]dioxin-2-carbonyl) piperazine having a purity of >99.9%.
REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 10 OF 36 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:390003 CAPLUS
DOCUMENT NUMBER: 138:386537
TITLE: Manufacture of water-based polyurethane dispersions for water-based contact adhesives
INVENTOR(S): Kitada, Mitsuru; Kuba, Kazuo; Hashimoto, Yutaka
PATENT ASSIGNEE(S): Dainippon Ink and Chemicals, Inc., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 11 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2003147041	A	20030521	JP 2002-174241	20020614
PRIORITY APPLN. INFO.:			JP 2001-257240 A	20010828

AB The process involves (i) mixing (A) water-based dispersions prepared by machine emulsification and dispersing of water-based solns. containing prepolymers prepared by reacting polyisocyanates and polyols with OH value 10-350 mg-KOH/g at NCO/OH = 2.00-1.01:1.00 (equivalent ratio) in organic solvents and ≥1 surfactants selected from metal salts or organic salts of dialkylsulfosuccinic acids and alkylbenzenesulfonic acids with (B) polyamines with mol. weight ≤300 and containing ≥2 functional groups at ratio amine value/NCO ≤1.9 (equiv), followed with chain-extending reaction, wherein at least 1 of polyols and polyamines contain carboxylate groups and/or sulfonate groups, average particle diameter of obtained polyurethane water-based dispersions being ≤1 μm with standard deviation ≤1 μm. Thus, 30 parts di-Me 5-sodiosulfoisophthalate-1,6-hexanediol-ε-caprolactone copolymer (reaction ratio 1480:1240:2280, OH value 120 mg-KOH/g, acid value 0.3 mg-KOH/g, theor. sulfonic acid metal salt group content 1080 mmol/kg) was reacted with 34 parts IPDI and 4 parts HDI in MEK at 80°, thinned with MEK, reacted with 5 parts 1,4-butylene glycol and 160 parts 1,4-butylene glycol-adipic acid copolymer (OH value 37) at 80° until NCO value reached ≤0.79%, cooled, emulsified in 280 parts water containing 1.7 parts Neocol YSK (dialkylsulfosuccic acid ester Na salt) under machine force, emulsified by adding a piperazine solution, and treated for solvent removal and to give a 50%-nonvolatile water dispersion. An adhesive comprising the dispersion 100, a thickener 1, CR 60N (water-dispersing NCO hardener) 3 parts, applied on 2 pieces of PVC sheets which were

subsequently bonded together under pressure to give test pieces having high adhesion strength.

L12 ANSWER 11 OF 36 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:309250 CAPLUS
DOCUMENT NUMBER: 138:321295
TITLE: Process for preparing (piperazinylmethyl)benzoic acid derivatives
INVENTOR(S): Takesaki, Hiroshi; Kitagawa, Satoshi; Matsuoka, Shotaro
PATENT ASSIGNEE(S): Toray Industries, Inc., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 7 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2003119184	A	20030423	JP 2001-314502	20011011
PRIORITY APPLN. INFO.:			JP 2001-314502	20011011
OTHER SOURCE(S):	MARPAT 138:321295			

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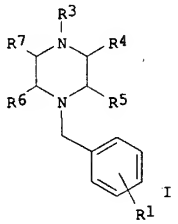
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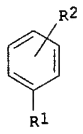
II

AB In the preparation of the title compds. I [R1 = carboxyl, etc.; R3 = alkyl, etc.; R4 - R7 = H, Me, etc.] by reaction of II [R1 = carboxyl, etc.; R2 = mono-substituted methyl; R2 is ortho, meta, or para to R1] with piperazine derivs. (III), the amount of III is ≥ 5 equiv relative to II. I are useful as pharmaceutical intermediates. 4-(4-Methylpiperazino)methylbenzoic acid.2HCl.1/2 H2O (with 98% purity) was prepared in 80% yield by the title process from p-(chloromethyl)benzoic acid and 1-methylpiperazine.

L12 ANSWER 12 OF 36 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:282146 CAPLUS
DOCUMENT NUMBER: 138:304301
TITLE: Novel synthesis and crystallization of piperazine ring-containing compounds such as mirtazapine
INVENTOR(S): Singer, Claude; Liberman, Anita; Finkelstein, Nina
PATENT ASSIGNEE(S): Israel
SOURCE: U.S. Pat. Appl. Publ., 9 pp., Cont.-in-part of U.S. Ser. No. 552,485.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003069417	A1	20030410	US 2002-206344	20020729
CN 1679586	A	20051012	CN 2005-10004288	20000418
CN 1680374	A	20051012	CN 2005-10004289	20000418
CN 1680365	A	20051012	CN 2005-10004290	20000418
US 2001051718	A1	20011213	US 2001-900646	20010706
US 6545149	B2	20030408		
US 2003088094	A1	20030508	US 2002-283093	20021030
US 6576764	B2	20030610		
US 2003120068	A1	20030626	US 2003-348757	20030123
US 2003135043	A1	20030717	US 2003-368441	20030220
US 2004176591	A1	20040909	US 2004-800918	20040316
AU 2005201117	A1	20050407	AU 2005-201117	20050315
PRIORITY APPLN. INFO.:			US 1999-130047P	P 19990419
			US 2000-182745P	P 20000216
			US 2000-552485	A2 20000418
			AU 2000-43577	A3 20000418
			CN 2000-807574	A3 20000418
			US 2001-900646	A3 20010706
			US 2002-283093	A3 20021030
			US 2003-368441	B1 20030220
OTHER SOURCE(S):	CASREACT 138:304301; MARPAT 138:304301			

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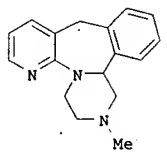
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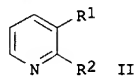
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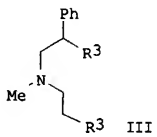
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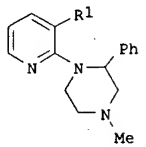
IV

AB Mirtazapine (I) was prepared by reacting substituted pyridine II [R1 = CH2OH, CH2Cl, CH2Br, CH2I; R2 = NH2] with compound III [R3 = Cl, F, Br, I] followed by treating the resulting piperazine IV with ring closing reagent, such as H2SO4. The mirtazapine intermediate IV (R1 = CO2H) may be prepared by hydrolyzing IV (R1 = CN) with KOH at a temperature of at least about 140°C. New processes for recrystn. of I form crude mirtazapine are also disclosed. The present invention also relates to crystalline adducts of mirtazapine and water, preferably containing up to about 3.5% by weight water, pharmaceutical compns. containing the crystalline adducts, and methods of treating depression by administering such compns.

L12 ANSWER 13 OF 36 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2003:239870 CAPLUS
DOCUMENT NUMBER: 138:256253
TITLE: Manufacture of stable aqueous dispersion of polyurethane resins for contact adhesives
INVENTOR(S): Kitada, Mitsuru; Kuba, Kazuo; Hashimoto, Yutaka
PATENT ASSIGNEE(S): Dainippon Ink and Chemicals, Inc., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 12 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2003089713	A	20030328	JP 2001-283129	20010918

PRIORITY APPLN. INFO.: JP 2001-283129 20010918

AB The process comprises (i) prepolymer formation from polyisocyanates, polyols (A) with OH value 10-350 mg-KOH/g, and optionally polyols (B) with Mw ≤300 by reaction at NCO/OH equivalent ratio 1.01-2.00 in organic solvents, (ii) phase-transfer emulsification by addition of aqueous surfactants chosen from metal/organic salts of dialkyl sulfosuccinate esters and/or alkylbenzenesulfonic acids to the prepolymers, and (iii) chain extension of the prepolymers by adding polyamines (d.p. ≤300) at amine/NCO equivalent ratio ≤1.9 to give aqueous dispersion of polyurethane resins, where the polyols and/or polyamines have carboxylate or sulfonate groups. Thus, a polyester polyol, prepared by polymerization of di-Me 5-sodiosulfoisophthalate with 1,6-hexanediol and then with ε-caprolactone, was reacted with IPDI, HMDI, 1,4-butylene glycol, and adipic acid-1,4-butylene glycol copolymer to give a polyester-polyurethane, which was mixed with Neocol YSK (sodium dialkyl sulfosuccinate) for emulsification and reacted with piperazine to give an emulsion with particle diameter 0.3 μm and good storage stability. Two PVC sheets were coated with an adhesive from the dispersion, heat treated, and press bonded, showing initial 180° peel strength 80 N/20 mm.

L12 ANSWER 14 OF 36 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:221692 CAPLUS
DOCUMENT NUMBER: 138:239702
TITLE: Production of solutions of highly purified triethylenediamine
INVENTOR(S): Lang, Ortmund; Rumpf, Bernd; Frauenkron, Matthias; Manderbach, Thomas; Stein, Bernd
PATENT ASSIGNEE(S): BASF Aktiengesellschaft, Germany
SOURCE: PCT Int. Appl., 23 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003022851	A1	20030320	WO 2002-EP10197	20020911
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
DE 10145117	A1	20030403	DE 2001-10145117	20010913
AU 2002339559	A1	20030324	AU 2002-339559	20020911
EP 1427731	A1	20040616	EP 2002-777064	20020911
EP 1427731	B1	20060510		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
CN 1553914	A	20041208	CN 2002-817896	20020911
JP 2005507879	T	20050324	JP 2003-526925	20020911
AT 325797	T	20060615	AT 2002-777064	20020911
ES 2263821	T3	20061216	ES 2002-2777064	20020911
US 2004220405	A1	20041104	US 2004-488978	20040309
US 7151177	B2	20061219		

PRIORITY APPLN. INFO.: DE 2001-10145117 A 20010913
WO 2002-EP10197 W 20020911

AB Highly purified triethylenediamine is obtained in a process comprising (a) separating crude triethylenediamine from high-boiling components, (b) evaporated triethylenediamine from the crude mixture, and (c) dissolving triethylenediamine in a solvent. A crystallization stage is absent in the process of the invention. The solns. of highly purified triethylenediamine can be used directly as catalysts in production of polyurethanes. Thus, triethylenediamine was produced by reacting ethylenediamine and piperazine in the presence of water . The reaction product mixture comprising ammonia (3), piperazine (17), triethylenediamine (23), water (54%) and high-boiling components and byproducts was subjected to distillation to remove low-boiling components, followed by distillation at 220° to sep. piperazine and triethylenediamine from high-boiling components. Piperazine was distilled off at 148° and in-process recycled. Triethylenediamine was evaporated and condensed at 30° in dipropylene glycol under falling film flow conditions, the resulting solution comprising piperazine (0.01), ethylpiperazine (0.01), triethylenediamine (34.0), dipropylene glycol (65.9%) and byproducts, to the balance.
REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 15 OF 36 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:97399 CAPLUS
DOCUMENT NUMBER: 138:153553
TITLE: A process for synthesis of antibiotic fluoroquinolonic acid derivatives
INVENTOR(S): Stankovic, Slobodan; Mitov, Slobodan; Stanojevic, Caslav
PATENT ASSIGNEE(S): Farmaceutsko-Hemijska Industrija "Zdravlje", Yugoslavia
SOURCE: PCT Int. Appl., 14 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003010144	A2	20030206	WO 2002-YU14	20020724
WO 2003010144	A3	20031016		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF,				

CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

AU 2002355298	A1	20030217	AU 2002-355298		20020724
PRIORITY APPLN. INFO.:			YU 2001-534	A	20010725
			WO 2002-YU14	W	20020724

OTHER SOURCE(S): CASREACT 138:153553; MARPAT 138:153553

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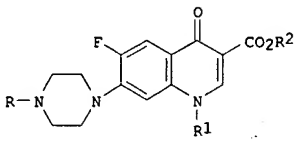

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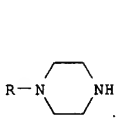

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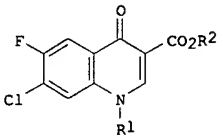

III

AB A simple and convenient procedure for obtaining antibiotics of fluoroquinolonic derivs. of general formula (I; where R, R2 = H, C1-4 alkyl; R1 = C1-4 alkyl, cycloalkyl such as cyclopropyl), and/or salts and hydrates thereof, in particular ciprofloxacin and norfloxacin, and is developed by amination of piperazine or piperazine derivs. (II; R = same as above) with the 6-fluoro-7-chloro-1,4-dihydro-4-oxoquinoline-3-carboxylic acid derivative of general formula (III; R1 , R2 = same as above) in an inert solvent of pharmacopoeic purity, at risen temperature The process is characterized in lower reaction temperature, atmospheric pressure reaction, tech. simplicity of the procedure of purification by conversion and isolation in the form of pharmaceutically acceptable salts, increased yields, reducing cost on the procedure for industrial use, as well as pharmacopoeic purity of the product, enabled their use as the antibiotics in human and veterinary medicine. Thus, a mixture of 49.25 g 7-chloro-1-cyclopropyl-6-fluoro-1,4-dihydro-4-oxoquinoline-3-carboxylic acid, 72.25 g piperazine, and 250 cm3 of DMSO was heated for 1.5 to 2 h at 140°, cooled to 70°, treated with 985 cm3 distilled water, and then treated with 62.5 cm3 concentrated HCl with stirring and cooling. Formed suspension was filtered and the precipitate was rinsed with distilled water, suspended in water, dissolved by addition of 2 mol/dm3 HCl, treated with active charcoal, heated with stirring at 50°, and filtered. To the filtrate was added 2 mol/dm3 NaOH with stirring and cooling and the formed suspension was filtered. The precipitate was rinsed with distilled water, suspended in water with stirring, treated with 60 cm3 2 mol/dm3 HCl, heated for 30 min at 75-80°, and added to 1,750 cm3 absolute ethanol. The mixture was cooled to 0-5° and filtered, and the precipitate was rinsed three times with 30 cm3 absolute ethanol each time, and dried in vacuum drier at 80° to give 49.46 g ciprofloxacin hydrochloride monohydrate (1-cyclopropyl-6-fluoro-1,4-dihydro-4-oxo-7-piperazinoquinoline-3-carboxylic acid hydrochloride monohydrate) as white crystals having m.p. 308-310° (decomposition) in 73% yield.

L12 ANSWER 16 OF 36 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2002:865553 CAPLUS

DOCUMENT NUMBER: 137:354699

TITLE: Extractive method for the recovery of high-purity triethylenediamine from mother liquor

INVENTOR(S): Lang, Ortmund; Rumpf, Bernd; Frauenkron, Matthias; Funhoff, Dirk; Manderbach, Thomas; Stein, Bernd

PATENT ASSIGNEE(S): BASF AG, Germany

SOURCE: Ger. Offen., 6 pp.
CODEN: GWXXBX

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 10122502	A1	20021114	DE 2001-10122502	20010510
US 2003004349	A1	20030102	US 2002-138337	20020506
EP 1258485	A1	20021120	EP 2002-10129	20020510
EP 1258485	B1	20050622		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
CN 1385430	A	20021218	CN 2002-117652	20020510
JP 2002363181	A	20021218	JP 2002-136221	20020510
AT 298340	T	20050715	AT 2002-10129	20020510
ES 2243619	T3	20051201	ES 2002-2010129	20020510

PRIORITY APPLN. INFO.: DE 2001-10122502 A 20010510

AB A procedure for the purification of triethylenediamine (TEDA) is described in which TEDA is vaporized from the mother liquor, the vaporous TEDA introduced into a liquid solvent from which it is subsequently crystallized, and the mother liquor contacted with extract the from which the crystallized TEDA is removed, the mother liquor extracted, and the TMEDA-free solvent recycled.

L12 ANSWER 17 OF 36 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2002:415324 CAPLUS

DOCUMENT NUMBER: 137:310893

TITLE: Diastereoselective Hydrogenation of Pyrazine Derivatives: An Alternative Method of Preparing Piperazine-(2S)-carboxylic Acid

AUTHOR(S): Kukula, Pavel; Prins, Roel

CORPORATE SOURCE: Laboratory for Technical Chemistry, Swiss Federal Institute of Technology (ETH), Zurich, CH-8093, Switz.

SOURCE: Journal of Catalysis (2002), 208(2), 404-411
CODEN: JCTLA5; ISSN: 0021-9517

PUBLISHER: Elsevier Science

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 137:310893

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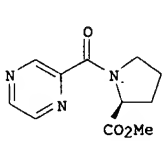

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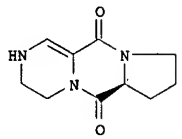


II

AB The diastereoselective hydrogenation of a chiral pyrazine derivative was used for the stereoselective preparation of piperazine-2-

carboxylic acid, which is an important chiral building block. The study was focused on the diastereoselective hydrogenation with various noble metal catalysts (Pd, Pt, Rh, Ru) on different supports. It was found that intramol. cyclization of the substrate (I) takes place during the hydrogenation, forming an unsatd. diketopiperazine derivative (II). This intermediate was further hydrogenated to a mixture of saturated heterocyclic diastereomers. The influence of the reaction conditions (temperature, pressure of hydrogen, and type of solvent) on the diastereoselectivity was also studied. The highest diastereoselectivity (79%) was reached with 10% Pd/C and with water as solvent. The desired mol. of piperazine-2-carboxylic acid was finally obtained by acidic hydrolysis of the diastereomeric diketopiperazine adduct.

REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 18 OF 36 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:31126 CAPLUS
DOCUMENT NUMBER: 136:86900
TITLE: Aqueous polyurethane adhesive compositions for artificial leather and manufacture of artificial leather using the same
INVENTOR(S): Satake, Eiji; Takeda, Shingo; Tanaka, Kazunori; Hashimoto, Yutaka
PATENT ASSIGNEE(S): Dainippon Ink and Chemicals, Inc., Japan
SOURCE: Eur. Pat. Appl., 14 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1170416	A2	20020109	EP 2001-115632	20010703
EP 1170416	A3	20040225		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002088662	A	20020327	JP 2001-192850	20010626
US 2002018892	A1	20020214	US 2001-895331	20010702
US 2003083432	A1	20030501	US 2002-238584	20020911
PRIORITY APPLN. INFO.:			JP 2000-203609 A	20000705
			US 2001-895331 A3	20010702

AB The composition containing no organic solvent, useful in a dry laminate process for manufacturing artificial leather, comprises (A) a water-borne polyurethane resin having softening temperature <80° and melt viscosity (at 80°) <105 Pa-s (e.g., adipic acid-diethanolamine-dimethylolpropionic acid-1,6-hexanediol-neopentyl glycol-piperazine-polypropylene glycol-tolylene diisocyanate block copolymer, triethylamine salt), (B) a crosslinking agent, and (C) a thickener (e.g., isophorone diisocyanate-polyethylene glycol copolymer derivs.), wherein softening temperature of the cured composition >120°. An artificial leather is manufactured by applying the aqueous adhesive composition onto a skin layer preformed on a release paper to give an adhesive layer; and dry laminating the adhesive layer with a base fabric material of a artificial leather.

L12 ANSWER 19 OF 36 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:870423 CAPLUS
DOCUMENT NUMBER: 136:167426
TITLE: Universal Solid-Phase Approach for the Immobilization, Derivatization, and Resin-to-Resin Transfer Reactions of Boronic Acids
AUTHOR(S): Gravel, Michel; Thompson, Kim A.; Zak, Mark; Berube, Christian; Hall, Dennis G.
CORPORATE SOURCE: Department of Chemistry, University of Alberta, Edmonton, AB, T6G 2G2, Can.
SOURCE: Journal of Organic Chemistry (2002), 67(1), 3-15
CODEN: JOCEAH; ISSN: 0022-3263
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 136:167426

AB Boronic acid-containing mols. are employed in a broad range of biol., medicinal, and synthetic applications. These compds., however, tend to be difficult to handle by solution-phase methods. Herein, this problem is addressed with the development of the first general solid-phase approach for the derivatization of functionalized boronic acids. This approach is based on the use of a diethanolamine resin anchor that facilitates boronic acid immobilization by avoiding the need for exhaustive removal of water in the esterification process. The immobilization of a wide variety of boronic acids onto N,N-diethanolaminomethyl polystyrene (DEAM-PS, 1) can be performed within minutes by simple stirring in anhydrous solvents at room temperature Evidence for the formation of a bicyclic diethanolamine boronate with putative N-B coordination was shown by 1H NMR anal. of DEAM-PS-supported p-tolylboronic acid. The hydrolytic cleavage of the same model boronic acid from the DEAM-PS resin was studied by UV spectroscopy. Hydrolysis and attachment were shown to occur under a rapidly attained equilibrium, and a large excess of water (>32 equiv) is required to effect a practically quant. release of boronic acids from DEAM-PS. Despite their relative sensitivity to water and alcs., DEAM-PS-bound arylboronic acids functionalized with a formyl, a bromomethyl, a carboxyl, or an amino group can be transformed in good to excellent yields into a wide variety of amines, amides, anilides, and ureas, resp. Ugi multicomponent reactions on DEAM-PS-supported aminobenzeneboronic acids, derivatization of multifunctional arylboronic acids, and sequential reactions can also be carried out efficiently. These new DEAM-PS-supported arylboronic acids can be employed directly into resin-to-resin transfer reactions (RRTR). This type of multiresin process helps eliminate time-consuming cleavage and transfer operations, thereby considerably simplifying the outlook of combinatorial library synthesis by manual or automated means. This concept was illustrated by a set of optimized procedures for the Suzuki cross-coupling and the borono-Mannich reactions.

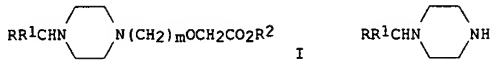
REFERENCE COUNT: 111 THERE ARE 111 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 20 OF 36 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:300697 CAPLUS
DOCUMENT NUMBER: 134:311229
TITLE: Process for preparing piperazine -substituted aliphatic carboxylates
INVENTOR(S): Hernandaz, Pedro E.; Fairfax, David E.; Michalson, Erik T.
PATENT ASSIGNEE(S): Salsbury Chemicals, Inc., USA
SOURCE: PCT Int. Appl., 18 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001029016	A1	20010426	WO 2000-US19625	20000719
W: JP				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				

US 6239277	B1	20010529	US 1999-421514		19991020
EP 1222179	A1	20020717	EP 2000-947505		20000719
EP 1222179	B1	20060621			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY					
AT 330945	T	20060715	AT 2000-947505		20000719
PRIORITY APPLN. INFO.:			US 1999-421514	A	19991020
			WO 2000-US19625	W	20000719

OTHER SOURCE(S): CASREACT 134:311229; MARPAT 134:311229
GI



I

II

AB Title compds. I (n = 1-6; R, R1 = H, alkyl, aryl, heteroaryl; R2 = branched alkyl or an organic or inorg. cation) were prepared by reaction of II (same R, R1) with X(CH2)nOCH2CO2R2 (X = a leaving group; same n, R2). Thus, 25 g of II (R = Ph, R1 = 4-ClC6H4) and 19.4 g ClCH2CH2OCH2COOCMe3, and 10.6 g Na2CO3 in 20 mL DMF were heated to 110° for 4 h. The resulting mixture was poured into water (50 mL) and extracted with toluene, and the solvent was removed to give tert-Bu cetirizine. Hydrolysis of the carboxylate with acid produces a piperazine-substituted aliphatic carboxylic acid or the acid salt thereof.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 21 OF 36 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:758131 CAPLUS
DOCUMENT NUMBER: 133:281797
TITLE: Synthesis of sildenafil
INVENTOR(S): Fu, Heliang; Wang, Xiaoyan; Pang, Baohua; Wang, Ning; Ji, Shangzhong
PATENT ASSIGNEE(S): Tianpu Biochemical Pharmaceutical Co., Ltd., Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, 14 pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

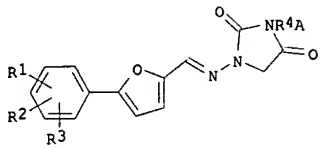
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 1246478	A	20000308	CN 1999-109552	19990712
CN 1092660	B	20021016		
PRIORITY APPLN. INFO.:			CN 1999-109552	19990712

OTHER SOURCE(S): CASREACT 133:281797
AB The process comprises methylating Et 3-propylpyrazole-5-carboxylate with di-Me sulfate at 90° for 2.5 h to obtain Et 1-methyl-3-propylpyrazole-5-carboxylate, hydrolyzing with 6M NaOH by refluxing for 3 h to obtain 1-methyl-3-propylpyrazole-5-carboxylic acid, nitrifying with fumed HNO3/fumed H2SO4 at 60° overnight, pouring into ice, filtering to obtain 1-methyl-4-nitro-3-propylpyrazole-5-carboxylic acid, chlorinating with SOCl2. By refluxing for 3 h, acylating with NH4OH to obtain 1-methyl-4-nitro-3-propylpyrazole-5-carboxamide, reducing with SnCl2 2H2O in 95% ethanol by refluxing for 2 h to obtain 4-amino-1-methyl-3-propylpyrazole-5-carboxamide, acylating with 2-ethoxybenzoyl chloride in dichloromethane in the presence of triethylamine and 4-dimethylaminopyridine for 2 h to obtain 4-(2-ethoxybenzamido)-1-methyl-3-propylpyrazole-5-carboxamide, sulfonating with Chlorosulfonic acid and SOCl2 for 18 h to obtain 4-ethoxy-3-(5-aminocarbonyl-1-methyl-3-propylpyrazol-4-yl)carbamoylbenzenesulfonyl chloride; acylating with piperazine in dichloromethane for 3 h to obtain 1-[4-ethoxy-3-(5-aminocarbonyl-1-methyl-3-propylpyrazol-4-yl)carbamoylbenzenesulfonyl] piperazine, cyclizing in organic solvent in the presence of base and peroxide at 50-170° for 2-72 h to obtain 1-[4-ethoxy-3-(6,7-dihydro-1-methyl-7-oxo-3-propyl-1H-pyrazolo[4,3-d]pyrimidin-5-yl)benzenesulfonyl] piperazine, and methylating with CH3I or di-Me sulfate in organic solvent in the presence of formaldehyde and formic acid at 0-120° for 1-48 h.

L12 ANSWER 22 OF 36 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1999:708766 CAPLUS
DOCUMENT NUMBER: 131:310639
TITLE: Process for making Azimilide dihydrochloride by sequential alkylation reactions of the 1-substituted 2,4-imidazolidinedione with 1,4-dihalobutane and N-methylpiperazine
INVENTOR(S): Matson, Patricia Ann; Godlewski, Michael Selden
PATENT ASSIGNEE(S): The Procter & Gamble Company, USA
SOURCE: PCT Int. Appl., 16 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9955701	A1	19991104	WO 1999-US9093	19990427
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2330685	A1	19991104	CA 1999-2330685	19990427
AU 9937644	A	19991116	AU 1999-37644	19990427
AU 747237	B2	20020509		
BR 9910078	A	20001226	BR 1999-10078	19990427
EP 1075474	A1	20010214	EP 1999-920062	19990427
EP 1075474	B1	20040908		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
TR 200003136	T2	20010321	TR 2000-200003136	19990427
JP 2002513022	T	20020508	JP 2000-545861	19990427
HU 200101356	A2	20020529	HU 2001-1356	19990427
RU 2194705	C2	20021220	RU 2000-129802	19990427
NZ 506773	A	20040326	NZ 1999-506773	19990427
AT 275563	T	20040915	AT 1999-920062	19990427
IL 138405	A	20050320	IL 1999-138405	19990427
TW 492965	B	20020701	TW 1999-88106940	19990728
EG 22464	A	20030226	EG 1999-1339	19991027
IN 2000DN00181	A	20051021	IN 2000-DN181	20000205
ZA 2000004714	A	20011120	ZA 2000-4714	20000907
MX 2000PA10534	A	20010507	MX 2000-PA10534	20001026
NO 2000005425	A	20001027	NO 2000-5425	20001027
US 6420568	B1	20020716	US 2000-674228	20001027
PRIORITY APPLN. INFO.:			US 1998-83406P P	19980429
			WO 1999-US9093 W	19990427

OTHER SOURCE(S): CASREACT 131:310639; MARPAT 131:310639
GI



I

AB A process for making 1,3-disubstituted-4-oxocyclic ureas of general formula (I): wherein R1, R2, and R3 are independently selected from the group consisting of nil, Cl, F, Br, NH2, NO2, COOH, CH3SO2NH, SO3H, OH, alkoxy, alkyl, alkoxycarbonyl, hydroxyalkyl, carboxyalkyl, and acyloxy; R4 is selected from the group consisting of a substituted or unsubstituted alkyl, alkenyl, alkynyl, alkylacyl, and heteroalkyl; and A is a substituted or unsubstituted, saturated or unsatd., straight-chain or branched alkyl or alkenyl amino group comprised of 1-7 carbon atoms; or A is a substituted or unsubstituted, saturated or unsatd. heterocycle having 5, 6, or 7 members containing at least one nitrogen, and R4 is attached to this nitrogen; wherein said 1,3-disubstituted-4-oxocyclic urea is made without isolation of intermediates and comprising the steps: (Ia) reacting a 1-substituted-4-oxocyclic urea with a carbon chain containing at least two leaving groups in the presence of a mild base and a solvent to form an adduct containing at least one leaving group, and (Ib) condensing the adduct with an amine to form a 1,3-disubstituted-4-oxocyclic urea, and (II) recovering said 1-3-disubstituted-4-oxocyclic urea, is disclosed. This method is particularly preferred for making 1-[[[5-(4-chlorophenyl)-2-furanyl]methylene]amino]-3-[4-(4-methyl-1-piperazinyl)butyl]-2,4-imidazolidinedione (Azimilide). Thus, e.g., 1-[[[5-(4-chlorophenyl)-2-furanyl]methylene]amino]-2,4-imidazolidinedione (300 g) was alkylated with 1-bromo-4-chlorobutane (187 g) in presence of potassium carbonate (219 g) in N-methylpyrrolidone (1.2 L); after stirring for 1 h at 70°, N-methylpiperazine (149 g) was added and the mixture stirred for approx. 150 min at 90°; workup and HCl treatment afforded 382.8 Azimilide dihydrochloride.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 23 OF 36 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1996:728679 CAPLUS
DOCUMENT NUMBER: 125:337040
TITLE: Phenolic novolak compositions and method for improving the green strength of refractory aggregate-binder mixtures, and the hardened carbonized compositions obtained
INVENTOR(S): Gerber, Arthur Harry
PATENT ASSIGNEE(S): Borden, Inc., USA
SOURCE: Eur. Pat. Appl., 17 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 736502	A2	19961009	EP 1996-301379	19960229
EP 736502	A3	19990203		
EP 736502	B1	20011114		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
US 5686506	A	19971111	US 1995-416192	19950404
AU 9640781	A	19961017	AU 1996-40781	19960103
AU 692636	B2	19980611		
CA 2166845	A1	19961005	CA 1996-2166845	19960109
ZA 9600369	A	19960801	ZA 1996-369	19960117
BR 9600241	A	19971223	BR 1996-241	19960126
JP 08283531	A	19961029	JP 1996-31825	19960220
JP 3693733	B2	20050907		
AT 208748	T	20011115	AT 1996-301379	19960229
CN 1134959	A	19961106	CN 1996-103983	19960329
US 5760104	A	19980602	US 1997-890202	19970709

PRIORITY APPLN. INFO.: US 1995-416192 A 19950404

AB The compns. consist of a binder comprising a solvent, especially furfuryl alc., a phenolic novolak binder resin dissolved in the solvent, and a chemical agent for improving the strength of Doloma (calcined dolomite) aggregate-containing greenware bonded by the binder. The chemical agent is selected from ≥1 of poly(dialkylaminomethyl)-substituted PhOH, poly(dialkylaminomethyl)-substituted bisphenol, N,N,N',N'-tetraalkyl-substituted diamines containing a C2-6-alkylene group between its N atoms, triethylenediamine, piperazine, ethylenediamine, poly(ethyleneamines), 1,3,5-trialkylhexahydro-s-triazines, formamide, (lower) alkoxymethylated melamine-H2CO polymers, tetramethylguanidine, glycerin, C3-6-alkyl-1,3-diols, and a chloride soluble in the binder. Optionally, the amine-containing chemical agents are at least partially neutralized with an acid. The binder contains approx. 2-10 weight% water and .ltorsim.4 weight% of a phenol. Bricks made from the Doloma aggregate mixed with the binder solution have good ambient-temperature green strength and enhanced modulus of rupture after curing and coking.

L12 ANSWER 24 OF 36 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1995:1002087 CAPLUS
DOCUMENT NUMBER: 124:71380
TITLE: Functional imaging with chemically amplified resists
AUTHOR(S): Vekselman, Alexander M.; Zhang, Chunhao; Darling Graham D.
CORPORATE SOURCE: Dep. Chemistry, McGill University, Quebec, H3A 2K6, Can.
SOURCE: ACS Symposium Series (1995), 614(Microelectronics Technology), 149-65
CODEN: ACSMC8; ISSN: 0097-6156
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The same dramatic photosensitivity shown by films of chemical amplified resists that permits their patterned removal ("relief development", typical of microlithog.), can also instead allow their further imagewise chemical modification ("functional development"), such as through exposure-controlled sorption of various species from contacting solns. or vapors. For example, radiation-defined deprotection of nonpolar poly(di-t-Bu fumarate-co-styrene) produced a pattern of polar and reactive carboxylic acid and anhydride moieties. Conditions were found for only these exposed areas of the resist material to take up Ca(II), Ni(II), Co(II), Pb(II) or some ammonium ions from the corresponding aqueous solns., without being dissolved. Several organic dyes were also placed into either exposed areas from water/alc. solns., or into unexposed areas from hexane/toluene solns. Modes and mechanisms are discussed in terms of resist, solute and solvent properties.

L12 ANSWER 25 OF 36 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1995:997344 CAPLUS
DOCUMENT NUMBER: 124:127124

TITLE: Aqueous solvent encapsulation method , apparatus and microcapsules
INVENTOR(S): Clark, Fred H.; Offit, Paul A.; Moser, Charlotte A.; Speaker, Tully J.
PATENT ASSIGNEE(S): Temple University, USA; Children's Hospital
SOURCE: PCT Int. Appl., 87 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9528227	A1	19951026	WO 1995-US4711	19950417
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TT				
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2187768	A1	19951026	CA 1995-2187768	19950417
AU 9523865	A	19951110	AU 1995-23865	19950417
EP 804283	A1	19971105	EP 1995-917018	19950417
EP 804283	B1	20030402		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT				
JP 10500889	T	19980127	JP 1995-527151	19950417
AT 235959	T	20030415	AT 1995-917018	19950417
HK 1001965	A1	20040709	HK 1998-100802	19980204
US 6531156	B1	20030311	US 1999-351370	19990712

PRIORITY APPLN. INFO.:

US 1994-228481	A	19940415
US 1994-229283	A	19940418
US 1994-229520	A	19940418
WO 1995-US4711	W	19950417
US 1997-809564	B1	19970324

AB A microcapsule substantially free of nonaq. contaminants comprises an aqueous core surrounded by a capsular wall, which is the reaction product of a selected water-soluble anionic polymer or salt thereof with a selected water-soluble amine or salt thereof. The selected anionic polymers and amines have the property that, when droplets of an aqueous solution of the selected polymer are introduced into an aqueous solution of the selected amine, stable microcapsules of the amine salt of the anionic polymer are formed. The aqueous core of the microcapsule may contain any of various active ingredients, including immunogenic agents such as rotavirus. A method and apparatus for making the microcapsules, as well as their method of use, are also disclosed. Tetracycline 15 mg was dissolved in 10 mL solution containing 0.06% Na alginate, then the solution was combined with 20 mL of a 0.05% aqueous solution of spermine HCl to form microcapsules containing tetracycline. The microcapsule suspension was centrifuged and the pelleted microcapsules were washed by resuspension in water. The supernatant liqs. obtained after 3 washes showed no significant absorbance characteristic of tetracycline.

L12 ANSWER 26 OF 36 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1994:630674 CAPLUS
DOCUMENT NUMBER: 121:230674
TITLE: Preparation of 7-amino-4-quinolonecarboxylic acids
INVENTOR(S): Ataka, Kikuo; Oku, Masayoshi; Kono, Masahiko; Matsuoka, Hiroko; Takama, Akira
PATENT ASSIGNEE(S): Ube Industries, Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 7 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 06157464	A	19940603	JP 1992-317659	19921127
JP 3275400	B2	20020415		

PRIORITY APPLN. INFO.: JP 1992-317659 19921127
OTHER SOURCE(S): CASREACT 121:230674; MARPAT 121:230674
GI For diagram(s), see printed CA Issue.
AB The title compds. I [R, R1 = substituent; A = divalent moiety; further details on said substituent and said divalent moiety are given], useful as bactericides (no data), are prepared by reaction of 6,7-difluoro-4-oxoquinoline-3-carboxylic acids with amines in the presence of trialkyl borates. A mixture of quinolone II, 1-(2-hydroxyethyl) piperazine, and tri-Bu borate in acetonitrile was refluxed for 5 h. After evaporation of the solvent and addition of water and HCl, crystals of quinolone III.HCl were obtained.

L12 ANSWER 27 OF 36 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1969:4143 CAPLUS
DOCUMENT NUMBER: 70:4143
TITLE: Azaspirodecanediones and azaspiroundecanediones
INVENTOR(S): Wu, Yao Hua
PATENT ASSIGNEE(S): Mead Johnson and Co.
SOURCE: U.S., 8 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 3398151	A	19680820	US 1967-607908	19670109

PRIORITY APPLN. INFO.: US 1967-607908 A 19670109
OTHER SOURCE(S): MARPAT 70:4143
GI For diagram(s), see printed CA Issue.
AB 8-(4-Phenyl-1-piperazinylalkylene)-8-azaspiro[4.5]decane-7,9-diones [I, n = 2, A = (CH2)x] having 0-3 substituents in the Ph ring were synthesized from the corresponding 4-phenylpiperazines and 3,3-tetramethyleneglutaric anhydride (II). Employing 3,3-pentamethyleneglutaric anhydride in the method yielded the 3-azaspiro[5.5]undecane-2,4-dione analog. These substances have strong activity and good selectivity in suppressing conditioned avoidance response in animals and are useful as psychotropic agents, analgetics, centrally acting muscle relaxants, capillary protectants, antiallergic agents, anti-inflammatory agents, and antiemetics. Thus, a mixture of 0.1 mole of the substituted glutaric anhydride, 0.1 mole 1-(ω-aminoalkyl)-4-phenylpiperazine, and 400 ml. C5H5N was refluxed 15 hrs., the solvent distilled, and the residue purified by distillation in vacuo or crystallization If the residue contained amide and carboxyl bands in the ir, it was refluxed with 10 parts by weight Ac2O for 15 hrs. prior to purification as above. The HCl salt of the free base was prepared by treating the EtOH solution of the free base with an equivalent amount of ethanolic HCl solution The following I were thus obtained (n A, R, b.p./mm. % yield, m.p. of HCl salt, and crystallization solvent given): 4, (CH2)2, H 215-35°/0.45, 80, 135-7° (decomposition), iso-PrOH; 4, (CH2)3, H, 250-2°/0.5, 80, 234.5-6.5° (decomposition), iso-PrOH-EtOH; 4, (CH2)4, H, 260-75°/0.1, 82.8, 218.5-20.5° (decomposition), iso-PrOH; 4, (CH2)5, H, 253-63°/0.2, 89, 188.5-96.5, EtOH; 5, (CH2)3, H, 263-76°/0.15-0.25, 77.8, 254-5°

(decomposition), EtOH; 5, (CH2)2, o-Me, 230-60°/0.2, 92, 211-12° (decomposition), EtOH; 4, (CH2)2, o-Me (III), 220-40°/0.35, 77, 196.5-8.5° (decomposition), EtOH); 4, (CH2)3, o-Me, 220-50°/0.11, 90, 208.5-10.5° (decomposition), iso-PrOH; 4, (CH2)2, m-Me, 225-35°/0.3, 81, 205.5-7.0° (decomposition), iso-PrOH; 4, (CH2)3, o-Cl, 215-45°/0.1, 94, 234.5-5.5° (decomposition), iso-PrOH; 4, (CH2)3, m-OMe, 200-60°/0.1, 70, 235.5-7.0° (decomposition), EtOH; 4, (CH2)2CHMeCH2, H, 235-50°/0.25, 80, 207.5-12.0°, iso-PrOH; 4, (CH2)4, o-OMe, 243-7°/0.18, 89.6, 199.5-203°, EtOH; 4, (CH2)4, o-Cl, 240-60°/-0.2, 90, 238.5-41.0°, EtOH; 4, (CH2)4, o-Me, 230-70°/0.1, 95, 202-3.5°, EtOH; 4, (CH2)4, o-Me, 255°/0.01, 86, 246-7.5°, EtOH; 4, (CH2)3, o-Me, 230-50°/0.3, 90, 254.5-5.5° (decomposition), iso-PrOH; 4, (CH2)5, o-OMe, -, 88, 174.5-6.5°, EtOH-Et2O; 4, (CH2)3, p-Me, 160-80°/0.1, 75, 247-8° (decomposition), iso-PrOH; 4 (CH2)2, p-Me, 165-200°/0.05-0.1, 73, 236.5-8.5° (decomposition), iso-PrOH; 4, (CH2)2, o-Cl, 165-84°/0.1, 80, 241-2.5° (decomposition), iso-PrOH; 4, (CH2)3, m-Cl, 164-70°/0.1, 68, 248.5-50.5° (decomposition), iso-PrOH; 4, (CH2)2, m-Cl, 140-210°/0.5-0.1, 74, 226.5-8.5° (decomposition), iso-PrOH; 4, (CH2)3, p-Cl, 175-97°/0.1, 90, 248-9° (decomposition), EtOH; 4, CHMeCH2, H, 230-40°/0.25, 87, 255.5-7.5°, EtOH. A stirred mixture of 19.2 g. 1-(o-methoxyphenyl)-piperazine (IV), 9.0 g. ClCH2CH2CN, 150 ml. C6H6, and 16.6 g. anhydrous Na2CO3 was refluxed overnight under anhydrous conditions and filtered, the filter cake washed with C6H6, and the combined C6H6 filtrates fractionally distilled in vacuo to give 19.6 g. 1-(2-cyanoethyl)-4-(o-methoxyphenyl) piperazine (V), b1 208-26°, m. 72-4°. A mixture of 8.1 g. V, 30 g. dry liquid NH3, and 100 ml. absolute MeOH was hydrogenated at 1200 psi. and room temperature over W-6 Raney Ni to give 85% 1-(3-aminopropyl)-4-(o-methoxyphenyl) piperazine (VI, A = (CH2)3, R = o-MeO). The following VI were similarly prepared (except that the last five compds. were prepared by reduction with LiAlH4, an example of which is given below) (A, R, % yield, b.p./mm., and n25D given): (CH2)2, m-Me, 85.5, 117-34°/0.3, 1.5638; (CH2)3, m-OMe, 68.8, 115-65°/0.15, 1.5561; (CH2)3, m-Me. 48.0, 120°/0.18, 1.5656; (CH2)3, m-Cl, 79, 142-70°/0.15-0.5, -; (CH2)3, m-Cl, 62, 108-40°/0.1-0.15, 1.5827; (CH2)2CNMeCH2, H, 81.7, 138-55°/0.17, 1.5485; (CH2)4, o-MeO, 79.6, 150-60°/0.25, 1.5496; (CH2)4, o-Cl, 74.0, 130-65°/0.15-0.35, 1.5560; (CH2)4, o-Me, 32.8, 145-60°/0.08, -; (CH2)5, o-MeO, 57.6, 163-72°/0.2, 1.5444. 1-(3-Cyano-2-methylpropyl)-4-phenylpiperazine, b0.15 155-68°, m. 81-3°, prepared in 65% yield from 3-chloro-2-methylbutyronitrile by the above procedure, was dissolved (0.04 mole) in 100 ml. tetrahydrofuran, the solution added dropwise with vigorous stirring during 35 min. to a suspension of 1.87 g. LiAlH4 in 100 ml. Et2O and refluxed, and the residue distilled in vacuo to give 81.7% 1-(4-amino-2-methylbutyl)-4-phenylpiperazine, b0.17 138-55°, n25D 1.5485. A stirred mixture of 16.8 g. II and 200 ml. C5H5N was treated with 12.2 g. ethanolamine, refluxed 3 hrs., and fractionally distilled in vacuo to give 12.0 g. 8-(2-hydroxyethyl)-8-azaspiro[4.5]decane-7,9-dione [(VII, A = (CH2)2, X = OH)] (VIIa), b0.05-0.1 142-50°, n25D 1.5150. A cooled mixture (10-15°) of 6.0 g. VIIa, 50 ml. C6H6, and 2.4 g. C5H5N was treated dropwise during 25 min. with 3.6 g. SOCl2, heated 1 hr. at 60-5°, and filtered, the filtrate treated with 20 ml. distilled H2O, and the C6H6 layer separated, dried, and fractionally distilled in vacuo to give 4.5 g. 8-(2-chloroethyl)-8-azaspiro[4.5]decane-7,9-dione [(VII, A = (CH2)2, X = Cl)] (VIIb), b0.05 120-2°, n25D 1.5139. The following VII were similarly prepared (A, X, b.p./mm., and % yield given); (CH2)3, OH, 155-70°/0.1-0.15, 62; (CH2)3, Cl, 155-62°/0.06, 73; (CH2)2O(CH2)2, OH, 191-204°/0.08-0.18, 80.7; (CH2)2O(CH2)2, Cl, 155-65°/0.25, 50; (CH2)4, OH, 185-240°/0.2, 74.9; (CH2)4, Cl, 160-95°/0.3, 53.5. A mixture of 23 g. VIIb, 19.2 g. IV, and 31.8 g. anhydrous Na2CO3, in 400 ml. C6H6 was refluxed 15 hrs., and filtered, and the filtrate fractionally distilled to give III. The following I were similarly prepared (n, A, R, b.p./mm., % yield, and m.p. of HCl salt given): 4, (CH2)3, p-MeO, 220-45°/0.1, 65, 225.5-6.5° (decomposition); 4, (CH2)2O(CH2)2, o-MeO, 240-60°/0.2, 20, 206.5-8.5°; 4, (CH2)2O(CH2)2, H, 190-260°/0.25-0.35, 86, 155-7°; 4, (CH2)3, m-Me, 160-85°/0.5-0.1, 92, 240.5-2.5° (decomposition); 4, (CH2)3, H, 240-60°/0.2, 69, 217.5-18.5°; 4, (CH2)4, o-F, -, -, 188-90°; 4, (CH2)4, o-MeSO2NH, -, 73.5, 263.5-4.5°; 4, (CH2)4, o-NO2, 150-80°/0.1, 26.8, -. I containing multiple substituents in the Ph ring were similarly prepared and were tabulated but not characterized. A mixture of 15.28 g. II, 200 ml. C5H5N, and 5.0 g. propargylamine was refluxed overnight in the absence of moisture and fractionally distilled in vacuo (b0.15 129-45°) to give crude 8-propargyl-8-azaspiro[4.5]decane-7,9-dione (VIII) contaminated with II. A mixture of 6.0 g. VIII, 2.4 g. 37% aqueous HCHO, a few crystals of CuCl (catalyst), 1.78 g. AcOH, 2.9 g. distilled H2O, and 4.8 g. 1-phenylpiperazine was heated under N on a water bath at 40° 7 hrs., extracted with 3 + 75 ml. CHCl3, and worked up in the usual manner, and the product converted to the HCl salt to give 6.5 g. 8-[4-(4-phenyl-1-piperazinyl)-2-butynyl]-8-azaspiro[4.5]decane-7,9-dione dihydrochloride, m. 173-4° (EtOH). Similarly prepared was 8-[4-(4-o-methoxyphenyl-1-piperazinyl)-2-butynyl]-8-azaspiro[4.5]decane-7,9-dione dihydrochloride, m. 172-5°.

L12 ANSWER 28 OF 36 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER:	1968:49647 CAPLUS
DOCUMENT NUMBER:	68:49647
TITLE:	Hydrazones of 1-amino-4-xanthenylcarbonylpiperazines
INVENTOR(S):	Cusic, John W.; Yonan, Peter
PATENT ASSIGNEE(S):	G.D. Searle and Co.
SOURCE:	U.S., 2 pp.
	CODEN: USXXAM
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	1
PATENT INFORMATION:	

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 3284449		19661108	US 1964-422057	19641229

GI For diagram(s), see printed CA Issue.

AB Hydrazones (I) have been prepared for pharmaceutical uses, e.g. anti-ulcer agents (activity demonstrated by their inhibition of ulceration in the Shay rat). Thus, 70 parts BuLi in heptane is added, with stirring, to a suspension of 232 parts 2-chlorothioxanthene in 1400 parts Et2O, the solution refluxed 3 hrs. and poured into a slurry of dry ice and Et2O, the mixture kept 15 hrs., KOH solution added to dissolve the precipitated carboxylic acid salt, and the aqueous layer separated and acidified with HCl to give 2-chlorothioxanthene-9-carboxylic acid (II), m. 225-7° (2-propanol). A suspension of 15 parts thioxanthene-9-carboxylic acid in 130 parts dry toluene is heated to reflux, 11.9 parts SOCl2 added, the mixture refluxed 2 hrs., solvent and excess SOCl2 are removed in vacuo, and hexane is added to the residue crystallize thioxanthene-9-carbonyl chloride (III) which is used without further purification. A solution is prepared from 102 parts xanthene-9-carbonyl chloride and 750 parts CHCl3 and 145 parts Et3N added slowly to this solution Some heat is generated during the process and the temperature rises to 50°. A solution of 50 parts 1-nitrosopiperazine in 150 parts CHCl3 is added portionwise the mixture refluxed 4 hrs. and cooled, an addnl. 375 parts CHCl3 added, and the solution worked up to give 1-nitroso-4-(xanthen-9-ylcarbonyl)piperazine (IV), m. 205-7° (CHCl3-Et2O), A solution of 35 parts IV in 470 parts glacial HOAc is heated to about 65° with stirring, and 82 parts water added, 50 parts Zn dust added portionwise at 60-5° over 30 min., and the mixture stirred

at 60-5° an addnl. 20 min., filtered, mixed with 500 parts cold H2O, made alkaline with NaOH solution, and worked up to give 1-amino-4-(xanthen-9-ylcarbonyl)piperazine (V), m. 147-50°. V (3.5 parts) is dissolved in 25 parts 2-propanol, 2 parts 4-pyridinecarboxaldehyde and 1 drop glacial HOAc are added, and the mixture is heated on a steam bath 4 min., cooled, and stirred to induce crystallization to give 1-(4-pyridylmethyleneamino)-4-(xanthen-9-ylcarbonyl) piperazine, m.-213-14°. In like manner the following 4-xanthen-9-ylcarbonyl-piperazine derivs. were prepared (substituted and m.p. given): 1; benzylideneamino, 146-7°; 1-piperonylideneamino, 194-5° 1-(fluoren-9-ylideneamino), 193-4°.

L12 ANSWER 29 OF 36 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1966:447695 CAPLUS
DOCUMENT NUMBER: 65:47695
ORIGINAL REFERENCE NO.: 65:8907b-h,8908a-h,8909a-h,8910a
TITLE: Agents acting on the central nervous system. V. 2 (and 3)-(Tertiary amino)-3-phenyl-, 3-(tertiary amino)-2-phenyl-, 2,3-di-(tertiary amino)-3-phenylpropionic acid esters and propanols and 1,2-and 1,3-di(tertiary amino)-3-phenylpropanes
AUTHOR(S): Kapil, R. S.; Gautam, B. C.; Vohra, M. M.; Anand, Nitya
CORPORATE SOURCE: Central Drug Res. Inst., Lucknow
SOURCE: Indian Journal of Chemistry (1966), 4(4), 177-87
CODEN: IJOCAP; ISSN: 0019-5103
DOCUMENT TYPE: Journal
LANGUAGE: English

AB cf. CA 62, 16231h. Condensation of methyl 2-bromo-3-aryl-propionates (I) with the appropriate amines in solvents of different polarity gave Me 2-(tertiary amino)-3-arylpropionates (II). I were prepared by adding the appropriate benzyl chloride (1 mole) to NaCH(CO2Et)2 in absolute EtOH under stirring and refluxing for 2 hrs.; stirring and refluxing were continued 24 hrs. to yield the ethyl benzylmalonate (a small amount of the corresponding ethyl dibenzylmalonate was also obtained) which was saponified with aqueous KOH and the acid liberated taken up in ether, and brominated by treatment with 1.1 moles Br in the cold; the α-bromobenzyl-malonic acid obtained was decarboxylated by heating 2-3 hrs. at 185-9°. Esterification of the acid with MeOH and HCl yielded the desired I. The following compds. were prepared: 2-bromo-3-(p-tolyl)propionic acid, m. 91-2° (methyl ester b3 136°, n30D 1.528); ethyl bis(4-chlorobenzyl)malonate, m. 102 °; methyl 2-bromo-3-(p-chlorophenyl)propionate, b3 133° , n30D 1.542; methyl 2-bromo-3-(m-chlorophenyl)propionate, b5 144°, n28D 1.544. 2-Bromo-3-phenylpropionic acid (35.7 g.) was added to 93.13 g. piperidine in 155 g. H2O, the solution kept 1 hr. at room temperature and evaporated in vacuo to dryness, and the residue repeatedly extracted with boiling EtOH to yield 12.5 g. 2-(1-piperidyl)-3-phenylpropionic acid, m. 213°; Me ester (IIa), b5 128° (method A). Alternatively, 170 g. piperidine was added dropwise (temperature <50°) to a solution of 243 g. methyl 2-bromo-3-phenylpropionate in 11. C6H6, the mixture kept 3 hrs. at <50°, the precipitated piperidine HBr filtered off, and the filtrate washed with H2O and extracted with 2N HCl. Working up of the COCH2 layer yielded 80 g. PhCH:CHCO2Me. The acid extract was basified (NH4OH), extracted with ether, and the ether extract dried and distilled to yield 62 g. IIa (method B). When, on the other hand, the reaction mixture was kept 24 hrs., the HCl salt of the product was found to be a mixture of IIa.HCl (major fraction) and HCl salt of methyl 3-(1-piperidyl)-3-phenylpropionate, m. 192°. Alternatively, 12.1 g. methyl 2-bromo-3-phenylpropionate and 18 g. C5H5N in 25 ml. MeOH was heated 4 hrs. (steam bath) and the solvent removed in vacuo to yield 14 g. 1-(1-methoxycarbonyl-2-phenyl)ethylpyridinium bromide, m. 155° which was dissolved in MeOH and added to pre-heated PtO2 and shaken until absorption of 3 moles H was complete. Working up of the reaction mixture yielded IIa. HBr (method C). II were also prepared as follows: a solution of 6.3 g. methyl phenylalaninate in 50 ml. tetrahydrofuran and 6.0 g. (CH2)2Br2 was refluxed 12 hrs., the solvent removed in the vacuo, and the residue treated with H2O and taken up in C6H6. The C6H6 layer was extracted with 2N HCl and the acid layer basified to yield 20% IIa. R, R1, R2, X, Method, %, yield, b.p./m.m., or m.p.; 1-pyridinium bromide, H, H, CO2Me, C, 88, 155°, (decompu.); 1-piperidyl (IIa), H, H, CO2Me, C, 90, 160°/3, (167° HCl, salt); 1-piperldyl, HBr salt, H, H, CO2Bu, C, 60, 164°; 1-pyrrolidyl, H, H, CO2Me, B, 35, 158°/5; 4-morpholinyl, H, H, CO2Me, B, 38, 186-8°/5, (190° HCl, salt); 4-(N-methylpipera-, zinyl), H, H, CO2Me, B, 20, 170°/5, 190° (HCl, salt); 1-(2 methylpiperidyl), HBr salt, H, H, CO2Me, C, 58, 166-7°; 1-piperidyl, H, H, CO2Me, C, 85, 150°/0.01, (165° HCl, salt); 1-piperidyl (IIb), H, H, CO2H, -, 60, 265° (233° HBr, salt); 1-piperidyl, HCl salt, (IIc), OH, H, CO2Me, -, 78.6, 252-3°; 1-pyrrolidyl, OMe, H, CO2Et, A, 40, -; 1-pyridinium bromide, Cl, H, CO2Me, C, 85, 96°; 1-piperidyl, HBr salt, Cl, H, CO2Me, C, 85, 205°; 1-pyridinium bromide, H, Cl, CO2Me, C, 85, 152°; 1-piperidyl, HBr salt, H, Cl, CO2Me, C, 88, 170°, (decomposition); 1 pyridinium bromide, Me, H, CO2Me, C, 80, 79°; 1-piperidyl, HBr salt, Me, H, CO2Me, B, 90, 207° The II (4,3-R R1R2C6H3CHXR) listed in the 1st table were prepared IIb was prepared by refluxing 6-8 hrs. a solution of 0.01 mole Me 2-(1-piperidyl)-3-(p-methoxyphenyl)propionate in 15 ml. 48% HBr, the excess HBr removed in vacuo and the sirnpy residue crystal, from MeOH-ether and then from H2O. IIc was prepared by adding dropwise (30 min.) 0.012 mole SOCl2 to a cooled (-10 to -15°) suspension of 0.01 mole 2-(1-piperidyl)-3-(phydroxyphenyl)propionic acid in 15 ml. dry MeOH, the reaction mixture stirred 2 hrs., refluxed 30 min., and worked up. 2-(Tertiary amino)-3-arylpropanols (III) were prepared as follows: methyl 2-(1-piperidyl)-3-phenylpropionate (12.48 g.) in 25 ml. ether was added dropwise under stirring to a suspension of 3.8 g. LiAlH4 in 200 ml. dry ether. After 3 hrs., the complex was treated with AcOME, H2O, and 40% NaOH successively and the reaction mixture worked up to yield 2-(1-piperidyl)-8-phenylpropanol (IIIa) (method A). When, on the other hand, the ester used for reduction was prepared by the reaction of the bromo ester with piperidine at >80° and(or) a long reaction time, the HCl salt obtained was a mixture, which could be separated by fractional crystallization into the HCl salt of IIIa and 3-(1-piperidyl)-3-phenylpropanol (Va) hydrochloride. Alternatively, 1.17 g. phenylalaninol (prepared by LiAlH4 reduction of the corresponding methyl phenylalaninate) in 20 ml. PhMe and 1.78 g. (CH2)2Br2 was refluxed 1 hr., the mixture heated for an addnl. 20 hrs. after adding 3 g. NaHCO3, cooled, treated with 20 ml. 5% NaOH, the PhMe layer separated, and the aqueous solution extracted with ether. The combined organic extract was washed with H2O, and extracted with dilute HCl. The acid extract was treated with 0.1 g. NaNO2 and basified to yield IIIa (method B). The III (4,3-R1R2C6H4CH2CHRCH2OH) listed in the 2nd table were prepared The m.p. of IIIc was reported incorrectly (J. Sci. Ind. Res. (India) 20B, 136(1961)) as 175°. R, R1, R2, Method, %, yield, b.p./mm., or m.p.; 1-piperidyl (IIIa), H, H, A, B, 95, 60, 48°, (207° HCl salt); 1-pyrrolidyl, H, H, A, 95, 164°/4; 4-(N-methylpiperazinyl, H, H, A, 92, 53°; 1-(2-methylpiperidyl), H, H, A, 89, 165°/0.01; 1-piperidyl(IIIc), OMe, H, A, 91, 160-5°/0.01, (212° HCl salt); 1-piperidyl, HCl salt, OH, H, A, 95, 205°; 1-pyrrolidyl, OMe, H, A, 94, 156°/2.7; 1-piperidyl, HCl salt, Cl, H, A, 88.5, 200°; 1-piperidyl, HCl salt, H, Cl, A, 83.3, 184° 1-pyridyl, Me, H, A, 72.7, 43-4°; 2-dibydroindolyl (IIIb), H, H, A, 30 98° 2-(1-Piperidyl)-3-(3-indolyl) propanol, m. 105°, was prepared by treatment of (CH2)5Br2 with tryptophanol as in method B except that tetrahydrofuran

(THF) was used as a solvent for condensation and treatment of the acidic extract with NaNO2 was omitted. D-and L-Phenylalaninols were prepared from the corresponding Me esters by reduction with LiAlH4 and converted into the corresponding piperidyl compds. by treatment with (CH2)5Br2 as described above. The following compds. were prepared (compound, % yield, m.p., and [α]21D given): L-phenylalaninol, 60, 96°, 22.9° (c 3.36, MeOCH); L-phenylalaninol, 62, 95°, -23.3° (c 2.01, MeOH); b-2-(1-piperidyl)-3-phenylpropanol, 62, 49° (HCl salt m. 210°), 11.0° (c 2.5, MeOH); L-2-(1-piperidyl)-3-phenylpropanol, 68, 49° (HCl salt m. 208°), -10.5° (c 2.72, MeOCH). 3-(Tertiary amino)-3-phenylpropionic acid esters (IV) were prepared as follows: a mixture of 1 mole PhCH:CHCO2Me, 4 moles piperidine and PhMe (6 ml./g. ester) was refluxed 12 hrs., cooled, the PhMe layer separated, washed with H2O, and extracted with 2N HCl. Basification of the acid extract and extraction with ether yielded Me 3-(1-piperidyl)-3-phenylpropionate (IVa). R, R1, R2, X, %, yield, b.p./mm., or m.p.; 1-piperidyl (IVa), H, H, CO2Me, 43, 172°/5, (192° HCl, salt); 1-piperidyl IVb), H, H, CONC8H10, -, 87° (211° HCl, salt); 1-pyrrolidyl, H, H, CO2Me, 49, 144°/3, 181° (HCl, salt); 4-morpholinyl, H, H, CO2Me, 30.1, 176-8°/5, (224° HCl, salt); 4-(N-methylpiperazinyl), H, H, CO2Me, 25.1, 176°/4; 1-homopiperidyl, H, H, CO2Me, 28, 180°/6, (decomposition), (177° HCl, salt); 1-piperidyl, HCl salt, Cl, H, CO2Me, 50.9, 202°; 1-pyrrolidyl, HCl salt, Cl, H, CO2Me, 37.9, 201°; 4-morpholinyl, Cl, H, CO2Me, 7.4, 165°/0.01; 1-piperidyl, OMe, H, CO2Me, 39.4, 160-69°/0.01, (182° HCl, salt); 1-pyrrolidyl, HCl salt, OMe, H, CO2Me, 38.1, 186°; 1-morpholinyl, OMe, H, CO2Me, 25, 156°/0.01; 1-piperidyl, HCl, salt, (IVd.), OMe, OMe, CO2Me, 28, 205°; 1-pyrrolidyl, HCl salt, OMe, OMe, CO2, 33.8, 186°; 1-piperidyl, HCl salt, -, -, CO2, 23.2, 72-3°; 1-pyrrolidyl, -, -, CO2Me, 18.4, 157-65°/0.01, (186° HCl, salt); 4-morpholinyl, HCl salt, -, -, CO2Me, 17.2, 219°; 4-(N-methylpiperazinyl), CHMe2, H, CO2Me, 26.3, 185-8°/3; 1-piperidyl, HBr, salt, (IVc.), OH, H, CO2H, 43, 170-1° N-[3-(1-Piperidyl)-3-phenylpropionyl]piperidine (IVb) was obtained from the residue left after distillation of IVa, by crystallization from MeOH.

The IV (4,3-R1R2C6H3CHRCH2X) listed in the 3rd table were prepared IVc was prepared by IVc was prepared by refluxing 6-8 hrs. a solution of 0.01 mole methyl 3-(1-piperidyl)-3-(p-methoxyphenyl)propionate in 15 ml. 48% HBr, the excess HBr removed in vacuo and the residue crystallized from MeOH-ether. Reduction of IV with LiAlH4 yielded 3-(tertiary amino)-3-arylpropanols (V). The V (4,3-R1R2C6H3CHRCH2CH2OH) listed in the 4th table were prepared Methyl 3-(1-piperidyl)-3-(α-furyl)propionate, b4 140°, n37D 1.483 [Pacheco, et al. (CA 58, 7933h) b3 140°] was prepared in 28% yield by heating methyl 3-(α-furyl)acrylate and piperidine as described for PhCH:CO2Me. R, R1, R2, %, yield, b.p./mm. or m.p., n35D; 1-piperidyl (Va), H, H, 95, 54° (135° HCl salt), -; 1-pyrrolidyl, H, H, 89.2, 146°/2.3, -; 4-morpholinyl, H, H, 83.7, 183°/4, 56°, 1.531; , , , , (207-9° HCl salt), ; 1-piperidyl, Cl, H, 86.1, 114° (142° HCl salt), -; 1-pyrrolidyl, Cl, H, 79.2, 168°/4, 1.542; 1-piperidyl, OMe, H, 74.5, 180°/4, 1.5350; 1-pyrrolidyl OMe, OMe, 82.4, 106°, -; 1-piperidyl, -, -, 81.7, 97° (205° HCl salt), -; 1-pyrrolidyl, -, -, 85.1, 185°/3, 1.5420; Similarly, methyl 3-(1-pyrrolidyl)-3-(α-furyl)propionate, b5 135°, n36D 1.4815 was prepared in 34% yield. LiAlH4 reduction of the above ester yielded 80% 3-(1-piperidyl)-3-(α-furyl)propanol, b6 150°; n35D 1.499. 3-(1-Pyrrolidyl)-3-(α-furyl)propanol, b4 139°, n34D 1.495 was similarly prepared 2(and 3)-(Tertiary amino)-3-phenylpropyl chlorides were prepared by heating 3 hrs. a mixture of 1 g. 3-(1-piperidyl)-3-phenylpropanol in 10 ml. C6H6 and 0.5 ml. SOCl2; the excess SOCl2 removed in vacuo and the residue crystallized from MeOH-ether. The chloride (1 mole) on heating 4 hrs. (steam bath) with 3 moles base (piperidine) and working up the reaction mixture yielded the corresponding 1,3-(and 1,2)-diarylaminophenylpropanes (VI). Alternatively, 1 g. IVb in 80 ml. ether was added dropwise to a stirred suspension of 0.75 g. LiAlH4 in 50 ml. ether, the mixture stirred 2 hrs. and worked up to yield 95% of the corresponding VI. R, R1, R2, m.p., (HCl salt), %, yield; Cl (VIa), H, 1-piperidyl, 183°, 65; Cl, H, 4-morpholinyl, 174°, 76; 1-piperidyl, H, 4-morpholinyl, 248°, 94; 4-morpholinyl, H, 4-morpholinyl, 346°, 98; 1-piperidyl, H, 1-piperidyl, 42° (di-HCl, salt 237°), 94; 4-morpholinyl, H, 1-piperidyl, 247°, 90; Cl, H, 1-piperidyl, 195°, 90; 1-piperidyl, 1-piperidyl, H, hygroscopic, 65; 4-morpholinyl, 1-piperidyl, H, hygroscopic, 60; 4-(N-phenylpiperazinyl), 1-piperidyl, H, hygroscopic, 55; The VI (PhCHR2CHR1CH2R)(isolated in the form of HCl salts) listed in the 5th table were prepared Methyl 2,3-di(tertiary amino)-3-phenylpropionates (VII) were prepared as follows: Methyl 2,3-dibromo-3-phenylpropionate (1 mole) (prepared by bromination of PhCH:CHCO2Me) and 4 moles of the appropriate secondary amine was dissolved in MeOH, the mixture heated 4 hrs. (water bath), the solvent removed in vacuo, and the residue diluted with H2O and extracted with ether. The ether extract was extracted with dilute HCl and the ether removed to give α-bromophenylcinnamate (VIII). The structure of VIII was established by its oxidation with KMnO4 to give BzH and by treatment with aqueous KOH to give phenylpropiolic acid. The following VII (PhCHRCHR1CO2Me) were prepared (R, R1, % yield, and m.p. given): 1-piperidyl, 1-piperidyl, 47, 129°; 1-pyrrolidyl, 1-pyrrolidyl, 49, 104°, 4-morpholinyl, -morpholinyl, 46, 163° and 105° (threo and erythro). The following PhCHRCHR1CH2OH were prepared by reduction of VII with LiAlH4 (same data given): 1-piperidyl, 1-piperidyl, 95, 97°; 1-pyrrolidyl, 1-pyrrolidyl, 92, 64°; 4-morpholinyl, 4-morpholinyl, 90, 124-5° and 122-3° (threo and erythro). VIa could be separated into threo and the erythro forms (m. 163° and 105°, resp.) either by fractional crystallization from EtOH or Me2CO or by column chromatography over silica gel and elution with C6H6 containing 5% CHCl3. Phenylmalonic acid (0.03 mole) was added gradually with occasional shaking to the base kept at 0° the mixture shaken 15 min., 3 ml. CH2O added, the mixture stirred 12 hrs. and concentrated in vacuo to yield the corresponding 3-(tertiary amino)-2-phenylpropionic acid PhCHR1CH2R2 (IX) (R2 = CO2H). SOCl2 (0.006 mole) was added dropwise with stirring during 0.5 hr. to a cooled (-15°) solution of 0.005 mole of the acid (IX, R2 = CO2H) in 15 ml. absolute MeOH. The reaction mixture was stirred 2 hrs. at room temperature, refluxed 30 min. and the solvent removed in vacuo to yield the corresponding esters (IX, R2 = CO2Me), which on LiAlH4 reduction yielded the resp. propanols (IX, R2 = CH2OH). R1, R2, % yield, m.p.; 1-piperidyl, CO2H, 40, 156°; 1-pyrrolidyl, CO2H, 39.6, 146°; 4-morpholinyl, CO2H, 38.2, 148°; 4-(N-methylpiperazinyl), CO2H, 37.3, 169°; 1-pyridyl, CO2Me, 86.6, 166°; 1-pyrrolidyl, CO2Me, 84.5, 152°; 4-morpholinyl, CO2Me, 79.4, 191°; 4-morpholinyl, CH2OH, 85, 132°; 1-piperidyl, CH2OH, 88, 114°; The IX listed in the 6th table were prepared The most active of these compds. were IIIa, IVd, and Va, which showed marked stimulant activity as evidenced by the increase in spontaneous activity and antireserpine activity. Their structure-activity relation is discussed.

L12 ANSWER 30 OF 36 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1964:484221 CAPLUS
DOCUMENT NUMBER: 61:84221
ORIGINAL REFERENCE NO.: 61:14665e-h,14666a
TITLE: Synthesis of some amides and amines containing the 1,4-benzodioxan nucleus as potential adrenolytic

agents
AUTHOR(S): Schreibman, M.; Miller, C. E.; Shelver, W. H.; Vacik, J. P.
CORPORATE SOURCE: North Dakota State Univ., Fargo
SOURCE: Journal of Pharmaceutical Sciences (1964), 53(8), 985-6
CODEN: JPMSAE; ISSN: 0022-3549
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
GI For diagram(s), see printed CA Issue.
AB A general method for the synthesis of 2-aminomethyl-1,4-benzodioxans (I) containing an aryl or heteroaryl substituent on the N was developed. 2-Hydroxymethyl-1,4-benzodioxan (25 g.) was mixed with 36 g. SOCl2, the mixture refluxed for 30 min., and excess SOCl2 removed by distillation to give 83% 2-chloromethyl-1,4-benzodioxan (II), b12 110-12°, n25D 1.5510. 2-Anilinomethyl-1,4-benzodioxan (III) was obtained from 10 g. I and 25 ml. PhNH2. The mixture was refluxed under N for 2 hrs., and excess PhNH2 removed by rendering the mixture basic with aqueous NaOH and steam distilling The residue was extracted with Et2O to give oily II; HCl salt m. 191-2°. The 1,4-benzodioxan-2-carboxamides (IV) were obtained from 1,4-benzodioxan-2-carbonyl chloride (V), prepared by Koo's method (CA 50, 8646c). Thus, V in 50 ml. benzene was added with stirring over 1 hr. to a solution of the appropriate amine in 150 ml. boiling benzene. The mixture was stirred and refluxed for 2 hrs., kept overnight, and treated with cold water to dissolve the precipitated amine salt. The benzene layer afforded IV, which were reduced with LiAlH4 to I. The following IV were prepared (amine, m.p., % yield, and recrystn. solvent given): aniline, 116-18°, 78, ligroine; 1-phenylpiperazine, 138-9°, 73, methylcyclohexane; 2-amino-4-methylpyridine, 109°, 67, EtOH-H2O; p-dimethylaminoaniline, 127-8°, 62, methylcyclohexane; p-phenylenediamine, 271-5°, 63, dioxane-H2O; trans-1-amino-4-methylcyclohexane, 209-10°, 63, EtOH; cis-1-amino-4-methylcyclohexane, 124-5°, 77, EtOH-H2O; diphenylamine, 127-8°, 89, EtOH-H2O; phenothiazine, 138-40°, 100, EtOH-H2O; p-nitroaniline, 179°, 100, C6H6. The following I HCl salts were prepared (data as above): aniline, 191-2°, 60, iso-PrOH; 1-phenylpiperazine, 240-4°, 37, Et2O-EtOH; p-dimethylaminoaniline, 195-9°, 43, Et2O-EtOH; p-phenylenediamine, 234-6°, 64, Et2O-EtOH-HCl; 1-amino-4-methylcyclohexane, 261-5°, 40, Et2O-EtOH.

L12 ANSWER 31 OF 36 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1955:24199 CAPLUS
DOCUMENT NUMBER: 49:24199
ORIGINAL REFERENCE NO.: 49:4730i,4731a-i,4732a
TITLE: Amino piperazines
INVENTOR(S): Conroy, Edward A.; Parker, Robert P.
PATENT ASSIGNEE(S): American Cyanamid Co.
DOCUMENT TYPE: Patent
LANGUAGE: Unavailable
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2663707		19531222	US 1951-233126	19510622

GI For diagram(s), see printed CA Issue.
AB Substituted N-aminopiperazines having central nervous system depressant, anticonvulsant, sedative, anesthetic or analgesic action are prepared RN.CHY1.CH2.NNHZ.CHY2.CH2 (I), where Z=H, Y1 and Y2 = Me or H, R = alkyl, aralkyl, monocyclic aryl, carbalkoxy, di-alkylcarbamyl, or heterocyclic radical. In the product, Z is a carbalkoxy, carbamoyl, thiocarbamoyl, or acyl radical. Method 1. 1-Carbethoxy-4-aminopiperazine (II) 35 and NaHCO3 21 parts in absolute EtOH 80 parts stirred below 50° while a solution of EtO2CCl (III) 21.5 in absolute EtOH 80 parts is added, the mixture refluxed 2 h., filtered, and the EtOH evaporated give Et N-(4-carbethoxy-1-piperazyl)carbamate, m. 143.5-4.5° (from Et2O). Method 2. II 34.6, Ac2O 20.5, and AcOH 150 parts heated (water bath) for 30 min., then poured into water 500 and concentrated ammonia 180 parts, the solution extracted with CHCl3 and the CHCl3 evaporated gives 1-carbethoxy-4-acetamidopiperazine, m. 180.5-1.0° (from acetone). Method 3. Ph isocyanate (IV) 75 in Et2O 75 parts added to II 26 in Et2O 150 parts over 10 min. at ice-bath temperature and the mixture filtered gives 1-phenyl-3-(4-carbethoxy-1-piperazyl)urea, m. 143.5-4.5° (from Me2CO-hexane). Method 4. Benzoyl chloride 28.1 added (10 min.) to a solution of 1-diethylcarbamoyl-4-aminopiperazine (V) 37 in 5% aqueous NaOH 150 parts, the mixture extracted with CHCl3, the CHCl3 evaporated gives 1-diethylcarbamoyl-4-benzoylaminopiperazine, m. 111-12° (from Me2CO-Et2O). The following list of products was also prepared The method number, starting material, other reactant, solvent, product, m. or b.p. of product, and crystallization solvent are given. 1, II, PhCH2COCl (VI), benzene, 1-carbethoxy-4-phenylacetyl-aminopiperazine, m. 138-9°, EtOAc; 3, II, cyclohexyl isocyanate (VII), Et2O, 1-cyclohexyl-3-(4-carbethoxy-1-piperazyl)urea, m. 159.5-60.5°, Me2CO-hexane; 3, II, PhNCS, Et2O, 1-phenyl-3-(4-carbethoxy-1-piperazyl)thiourea, m. 189-90°, EtOH; 3, II, allyl isothiocyanate (VIII), Et2O, 1-allyl-3-(4-carbethoxy-1-piperazyl)thiourea, m. 132-3°, Me2CO-hexane; 1, V, III, EtOH, Et N-(4-diethylcarbamoyl-1-piperazyl)carbamate, b5.0 200-5°, -; 2, V, Ac2O, AcOH, 1-diethylcarbamoyl-4-acetylaminopiperazine, m. 85.5-6.5°, Me2CO-Et2O; 3, V, IV, Et2O, 1-phenyl-3-(4-diethylcarbamyl-1-piperazyl)urea, m. 111-13°, Me2CO-hexane; 3, V, VII, Et2O, 1-cyclohexyl-3-(4-diethylcarbamoyl-1-piperazyl)urea, m. 98.0-9.5°, hexane; 3, V, EtNCS (IX), Et2O, 1-ethyl-3-(4-diethylcarbamoyl-1-piperazyl)thiourea, m. 146-7°, Me2CO-hexane; 4, V, 4-chlorobenzenesulfonyl chloride (X), 5% NaOH, N-(4-diethylcarbamoyl-1-piperazyl)-4-chlorobenzenesulfonamide, m. 150.5-1.5°, aqueous EtOH; 1, 1-methyl-4-aminopiperazine (XI), III, EtOH, Et N-(4-methyl-4-aminopiperazyl)carbamate, b3 122-4°; 3, XI, VII, Et2O, 1-cyclohexyl-3-(4-methyl-1-piperazyl)urea, m. 159.5-60.0°, Me2CO; 3, XI, IX, Et2O, 1-ethyl-3-(4-methyl-1-piperazyl)thiourea, m. 156.2-6.7°, Me2CO; 1, 1-benzyl-4-aminopiperazine (XII), III, EtOH, Et N-(4-benzyl-1-piperazyl)carbamate, m. 95.5-6.5°, hexane; 2, XII, Ac2O, AcOH, 1-benzyl-4-acetamidopiperazine, m. 136-7°, Me2CO; 4, XII, VI, benzene-pyridine, 1-benzyl-4-phenylacetamidopiperazine, m. 161.0-1.7°, Me2CO; 4, XII, BzCl, 5% NaOH, 1-benzyl-4-benzoylaminopiperazine, m. 173-4°, Me2CO; 3, XII, IV, Et2O, 1-phenyl-3-(4-benzyl-1-piperazyl)urea, m. 135.0-5.5°, aqueous EtOH; 3, XII, PhNCS, Et2O, 1-phenyl-3-(4-benzyl-1-piperazyl)thiourea, m. 180.5-82.0°, Me2CO-EtOH; 1, 1-(4-chlorophenyl)-4-aminopiperazine (XIII), III, EtOH, Et N-4-(4-chlorophenyl)-1-piperazylcarbamate, m. 194.5-5.5°, Me2CO; 2, XIII, Ac2O, AcOH, 1-(4-chlorophenyl)-4-acetyl-aminopiperazine, m. 211.5-13.0°, EtOH; 3, XIII, IV, Et2O, 1-phenyl-3-[4-(4-chlorophenyl)piperazyl] urea, m. 230.5-31.0°, PhCl; 3, XIII, o-ClC6H4NCS, Et2O, 1-(2-chlorophenyl)-3-[4-(4-chlorophenyl)-1-piperazyl]urea, m. 238.5-39.0°, CHCl3; 3, XIII, Et2NCOCl, Et2O, 1,1-diethyl-3-[4-(4-chlorophenyl)-1-piperazyl]urea, m. 108.5-9.0°, hexane; 3, XIII, VIII, Et2O, 1-allyl-3-[4-(4-chlorophenyl)-1-piperazyl]-thiourea, m. 198.5-200.0°, EtOH; 1, 1-(2-pyridyl)-4-aminopiperazine (XIV), III, EtOH, Et N-[4-(2-pyridyl)-1-piperazyl]carbamate, m. 133-4°, Et2O; 2, XIV, Ac2O, AcOH, 1-(2-pyridyl)-4-acetamidopiperazine, m. 172.5-3.5°, Me2CO; 3, XIV, IV, Et2O, 1-phenyl-3-[4-(2-pyridyl)-1-piperazyl]urea, m. 179.0-80.0°, Me2CO; 3, XIV, VIII, Et2O, 1-allyl-3-[4-(2-pyridyl)-1-piperazyl]thiourea, m. 155-6°, EtOH; 4, XIV, X, 10% aqueous NaOH, N-[4-(2-pyridyl)-1-piperazyl]-4-chlorobenzenesulfonamide, m. 173-4.5° (decompose), EtOH; 1, 1-(2-pyrimidyl)4-aminopiperazine (XV), III, EtOH, Et

N-[4-(2-pyrimidyl)-1-piperazyl]carbamate, m. 186.5-7.5°, EtOH; 2, XV, Ac2O, AcOH, 1-(2-pyrimidyl)-4-acetamidopiperazine, m. 248.0-9.5°, EtOH; 3, XV, VII, Et2O, 1-cyclohexyl-3-[4-(2-pyrimidyl)-1-piperazyl]urea, m. 200.5-1.5°, Me2CO; 3, XV, IX, Et2O, 1-ethyl-3-[4-(2-pyrimidyl)-1-piperazyl]thiourea, m. 206.5-8.0°, EtOH.

L12 ANSWER 32 OF 36 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1955:23966 CAPLUS
DOCUMENT NUMBER: 49:23966
ORIGINAL REFERENCE NO.: 49:4664b-i,4665a-h
TITLE: Unsymmetrically N-substituted piperazines. VI. Ester derivatives as spasmolytics
AUTHOR(S): Ide, Walter S.; Lorz, Emil; Baltzly, Richard
CORPORATE SOURCE: Wellcome Research Labs., Tuckahoe, NY
SOURCE: Journal of the American Chemical Society (1954), 76, 1122-5
CODEN: JACSAT; ISSN: 0002-7863
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
GI For diagram(s), see printed CA Issue.
AB cf. preceding abstract The preparation of a series of piperazino esters is described. None of these compds. showed a marked spasmolytic activity. 1-Benzylpiperazine (35.2 g.) in 100 cc. absolute EtOH treated at 0° with 8.8 g. ethylene oxide, the mixture warmed gradually to room temperature, allowed to stand 5 days, the EtOH distilled off at atmospheric pressure, and the residue distilled in vacuo yielded 42.6 g. (97%) 1-benzyl-4-(2-hydroxyethyl) piperazine (I), b2 142-3°. Piperazine (II) di-HCl salt (159 g.) in warm MeOH treated with 1 mole NaOMe, then with 109 g. EtBr, allowed to stand overnight, refluxed 1 hr., cooled, treated with 2 moles NaOMe, filtered, the filter cake washed with MeOH, the combined filtrate and washing treated with 52 g. ethylene oxide the mixture allowed to stand 3 days at room temperature; the solvent removed in vacuo, and the residue distilled gave 58 g. (37%) 1-Et analog of I, b25 125-30°; redistd., b21 128°. I.2HCl (159 g.) and 84 g. NaHCO3 heated in 1 l. MeOH until the CO2 evolution ceased, the mixture cooled, treated with 50 g. ethylene oxide, allowed to stand 4 days at room temperature, filtered, the filtrates and washings evaporated in vacuo on the steam bath, the residue treated with 53 g. NaHCO3 and 250 cc. H2O, the solution warmed on the steam bath, again evaporated in vacuo, the residue dissolved in the min. amount of H2O, the solution treated with 100 cc. 37% aqueous CH2O and 150 cc. 98% HCO2H, heated 4 hrs. on the steam bath, treated with 250 cc. concentrated HCl, evaporated in vacuo, the residue suspended in MeOH, the mixture saturated with NH3, treated with 0.77 mole NaOMe, filtered, and the filtrate distilled in vacuo yielded 66 g. 1-Me analog (III) of I, b9 103-5°. 1-(2-Hydroxyethyl)-4-(p-methoxybenzyl)piperazine, b2 182-3°, was prepared by the method of Staple and Wagner (C.A. 44, 5353g); di-HCl salt, m. 238°. Freshly prepared xanthydrol (19.8 g.), 10.4 g. NaCN, and 80 cc. glacial AcOH heated 24 hrs. in a glass-lined steel bomb at 100°, the mixture cooled, poured into 500 cc. ice water, filtered, the filter cake washed well with cold H2O, the solid (18 g.) refluxed with 20 g. KOH in 200 cc. 75% MeOH (by which time the evolution of NH3 ceased), the bulk of the MeOH boiled off, the residue diluted with H2O to 300 cc., filtered, extracted twice with Et2O, the cold aqueous layer acidified strongly with HCl, the precipitate taken into Et2O, the solution dried over Na2SO4, diluted with 100 cc. hexane, and evaporated gave 15.5 g. (68-9%) 9-xanthenecarboxylic acid (IV), m. 218-20°. Xanthydrol (0.05 mole), 0.06 mole NaCN, and 0.1 mole H2SO4 in 40 cc. glacial AcOH gave in a similar run 20% IV. The preparation of the desired esters was carried out by treating the appropriate acid chloride with 2 equivs. of amino alc. in Et2O or C6H6 and further purifying the ester base by partitioning between Et2O and aqueous Na2O3, drying over K2CO3, and converting to the di-HCl salt, or in some cases directly to the methiodide with MeI. IV (3.6 g.) refluxed with 6 g. SOCl2, the mixture evacuated on the steam bath, the residue dissolved in dry Et2O, the solution treated with 6 g. III, the mixture refluxed 4 hrs. and let stand overnight, the precipitate filtered off, and washed with Et2O, and the filtrate and washings partitioned against H2O until the aqueous layers were neutral, the Et2O layer extracted with N HCl, the aqueous layer basified with NaHCO3 and extracted with Et2O, and the extract dried with K2CO3 and evaporated gave 4.4 g. 2-(4-methylpiperazinoethyl)-9-xanthenecarboxylate which was dissolved in dry Et2O, and the solution divided into 2 equal parts; 1 part with excess alc. HCl gave the di-HCl salt, m. 227° (from absolute EtOH); the other part with MeI gave the methiodide, m. 191° (from EtOH-Et2O). I (11 g.) in 15 cc. dry C6H6 treated with 5.5 g. Ph2CHCOCl in C6H6, the solution warmed, the resulting gelatinous precipitate separated, treated with 50 cc. C6H6, broken up, and the mixture heated 5 min. on the steam bath, allowed to stand 2 hrs., partitioned between Et2O and dilute aqueous alkali, and the Et2O layer washed with H2O until the pH of the washings was 8, dried with K2CO3, and evaporated gave 10 g. 2-(4-benzylpiperazino)ethyl diphenylacetate (V), converted to the di-HCl salt, m. 235° (from EtOH-Et2O), and the methiodide, m. 182° (from EtOH-Et2O). Similarly were prepared the following compds. RCO2(CH2)2N.(CH2)2.NR'.CH2.CH2 (R, R', m.p. of the di-HCl salt and of the methiodide given): Am2CH, Me, 210° (from absolute EtOH-Et2O), 194° (from EtOH-Et2O); (C6H13)2CH, Me, 207° (from EtOH-Et2O), -; 1-phenylcyclohexyl, Me, 258° (from absolute EtOH), 198° (from absolute EtOH) [BuI derivative, m. 142° (from Me2CO)]; cyclohexylphenylmethyl, Me, 215° (from EtOH-Et2O), -; dicyclohexylmethyl, Me, 237° (from EtOH-Et2O), 222° (from EtOH-Et2O); Ph2CH, Me, crystallizing with 0.5 mole H2O, 218° (from iso-PrOH), -; Ph2C(OH), Me, 208° (from absolute EtOH), -; Ph2CHCH2, Me, 208° (from absolute EtOH), 142° (from absolute EtOH) [ethiodide, m. 81° (from EtOH-Et2O)]; 1-phenylcyclohexyl, Et, 230° (from EtOH-Et2O), -; cyclohexylphenylmethyl, Et, 201° (from absolute EtOH-EtOAc-Et2O), -; 9-fluorenyl, Et, 234° (from aqueous EtOH), -; Ph2CH, H, 179° (from iso-PrOH), -; Ph2C(OH), p-MeOC6H4CH2, 218° (from EtOH-Et2O), -. V (21 g.) in 100 cc. cold C6H6 heated 25.5 hrs. in a steel bomb with 20 g. MeBr, and the dirty-white precipitate washed with C6H6 and recrystd. from absolute EtOH gave V.2MeBr, m. 208°. V.MeI refluxed with excess MeI in iso-PrOH yielded V.gMeI, yellow crystals, decompose 199° (from MeOH-Et2O). V.2MeBr (5.2 g.) in aqueous MeOH hydrogenated over PtO2 at room temperature, the mixt.filtered, evaporated in vacuo below 60°, and the colorless crystalline residue recrystd. from MeOH-Et2O gave 1,4-dimethyl-1-[2-(diphenylacetoxy)ethyl]piperazinium bromide HBr salt (VI), m. 116°, which was probably a hydrate; it became sticky when dried in vacuo and then exposed to air, and finally became a dry solid again; 118 mg. lost in a high vacuum H2O corresponding to 2-2.5 equivs.; a sample kept in a vacuum desiccator 2 weeks gave analytical values slightly high for a monohydrate; these results indicate the existence of a monohydrate of a very high and higher hydrate of relatively low stability. 1-Methylpiperazine (VII) (4 g.) and 5.2 g. Ph2CHO2CCH2Cl in 15 cc. C6H6 refluxed 2 hrs. after the initial exothermic reaction, allowed to stand overnight, partitioned between Et2O and H2O, and the Et2O layer dried with K2CO3 and evaporated gave 6.5 g. residue which was converted to the di-HCl salt of benzhydryl 4-methyl-1-piperazineacetate, m. 186-7°. VII gave similarly with Ph(C6H11)CHO2CCH2Cl, followed by treatment with MeI, phenylcyclohexylcarbinyl 4-methyl-1-piperazineacetate-MeI, m. 207-8°. VII (4 g.) was added to 4.4 g. 1-C10H7NHCOCH2Cl in warm C6H6, the solution refluxed 20 min., cooled, diluted with dry Et2O, the precipitated VII.HCl filtered off, the Et2O filtrate dried with K2CO3, filtered, evaporated, and the residual oil (4.2 g.), which crystallized on standing, m. 122%,

converted to N-(1-naphthyl)-1-(4-methylpiperazine)acetamide-2HCl, decompose 233°. VII (8 g.), and 8.4 g. Me2CHCHBrCO2Et refluxed 32 hrs. in C6H6, the mixture partitioned between Et2O and H2O, the Et2O layer dried, acidified with alc. HCl, the resulting deliquescient di-HCl salt dissolved in H2O, basified with Na2CO3, extracted with Et2O, the extract dried with K2CO3 treated with EtI, and the crystalline deposit recrystd. from EtOH-Et2O gave N-methyl-N-ethyl-N'-(1-carbethoxyisobutyl)piperazinium iodide, m. 137-8°.

L12 ANSWER 33 OF 36 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1950:38157 CAPLUS
DOCUMENT NUMBER: 44:38157
ORIGINAL REFERENCE NO.: 44:7328h-i,7329a-g
TITLE: Histamine antagonists. III. 1- and 1,4-Substituted piperazine derivatives
AUTHOR(S): Hamlin, K. E.; Weston, Arthur W.; Fischer, Francis E.; Michaels, R. J., Jr.
CORPORATE SOURCE: Abbott Research Lab., Chicago
SOURCE: Journal of the American Chemical Society (1949), 71, 2734-6
CODEN: JACSAT; ISSN: 0002-7863
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
AB The synthesis of a number of 1-substituted, sym-1,4-disubstituted, and unsym-1,4-disubstituted piperazines as histamine antagonists is described. These compds. were prepared from I or piperazine (X) by one of 3 methods. 2,2-Diphenylethanol (XI) (93% from Ph2CHCO2H with LiAlH4), bl 144-5°, m. 54-5°; benzoate, m. 90-2°. Method A: 8.6 g. anhydrous X and 17.7 g. 1-C10H7CH2Cl in 150 cc. absolute EtOH were allowed to stand at room temperature for 17 hrs., the crystalline precipitate (XII) filtered off, the filtrate concentrated in vacuo, the residue made alkaline and extracted with ether, and the dried ether extract distilled to give 8.3 g. 1-(1-naphthylmethyl)piperazine (XIII), bl 154-6°; XIII.HCl, m. 227-8° (from EtOH). XII represented a 10-g. yield of 1,4-bis(1-naphthylmethyl)piperazine, m. 163-5°. 2-Bromopyridine (31.6 g.), 34.4 g. X, and 20 g. pyridine were heated for 6 hrs. in an autoclave at 155°, the mixture made strongly alkaline, extracted with ether, and the dried extract distilled; the fraction bl.4 114-16° (12.9 g.) was 1-(2-pyridyl)piperazine (XIV); XIV.HCl, m. 232-3° (from absolute EtOH); XIV.2HCl, m. 275-6° (from EtOH). The fraction bl.4 135-40° (7 g.) was 1,4-bis(2-pyridyl)piperazine (XV), m. 124-6° (from EtOH); XV.2HCl, m. 281-3° (from absolute EtOH). Method B: 1-(p-Bromobenzyl)piperazine-HCl (5 g.) in water was treated with 0.72 g. NaOH, 12.5 cc. anhydrous HCO2H and 2.5 cc. formalin added, the solution refluxed 4 hrs., concentrated in vacuo, the residue made alkaline and extracted with ether, and the dried exts. were treated with ethereal HCl to precipitate 5 g. 1-(p-bromobenzyl)-4-methylpiperazine-2HCl, m. 292-4° (from EtOH). Method C: 1-(2-Hydroxyethyl)piperazine (6.5 g.), 14 g. 1-C10H7CH2Cl, 5.3 g. Na2CO3, and 100 cc. anhydrous xylene were refluxed and stirred 18 hrs., the mixture cooled, acidified with concentrated HCl, the solvents removed in vacuo, the residue treated with solid NaOH, the oil extracted with ether, and the dried ether solution treated with ethereal HCl to precipitate 14 g. 1-(1-naphthylmethyl)-4-(2-hydroxyethyl) piperazine-2HCl, m. 206-6.5° (from EtOH-ether) (decomposition). I (15.8 g.), 27 g. 9-bromofluorene, and 5.8 g. Na2CO3 in 100 cc. BuOH were heated 4 hrs. on a steam bath, the mixture cooled and filtered, the crystals washed with BuOH, dissolved in dilute HCl, and washed with ether, and the acid layer made alkaline; the separated oil solidified to give 22 g. 1-(9-fluorenyl)-4-carboxypiperazine (XVI), m. 152-3° (from EtOAc); XVI.HCl, m. 219-20° (from EtOH-ether). XVI (10 g.) in 100 cc. concentrated HCl, refluxed 60 hrs. and concentrated in vacuo, yielded 7 g. 1-(9-fluorenyl)piperazine, m. 283-5° (decomposition) (from absolute EtOH). The consts. of the 1- and 1,4-substituted piperazines , RN(CH2.CH2)2NR', prepared are given below: R, R', Base B.p. °C., Mm., nD °C., Method, Yield %, Salt M.p. °C., Formula; p-BrC6H4CH2 Me, , , , , B, 86, 292-4, C12H17BrN2.2HCl; Ph2CHCH2, Me, , , , , C, 40, 278-9, C19H24N2.2HCl; Ph2C:CHCH2, Me, 167-70, 0.9, 1.5807, 30.5, C, 71, 139-40, C20H24N2.HCld; 1-C10H7CH2, H, 154-6, 1, , , A, 37, 227-8, C15H18N2.HCl; 1-C10H7CH2, Me, , , , , B, Quant., 241c, C16H20N2.2HCl; 1-C10H7CH2, CH2CH2OH, , , , , C, 81, 206-6.5c, C17H22N2O.2HCl; 1-C10H7CH2, 1-C10H7CH2, (m. 163-4.5), , , , A, 27, , C26H26N2; 2-C10H7CH2, H, 155-60, 1, 1.6101, 25, A, 33, 193-5, C15H18N2.HCl; 2-C10H7CH2, Me, , , , , B, 82, 281c, C16H20N2.2HCl; 2-C10H7CH2, CH2CH2OH, , , , , C, 33, 241c, C17H22N2O.2HCl; 2-C10H7CH2, 2-C10H7CH2, (m. 159-60.5), , , , A, 23, , C26H26N2; 9-C13H9a, H, , , , , .., 89, 283-5c, C17H18N2.2HCl; 9-C13H9, Me, , , , , C, 57, 265-8c, C18H20N2.2HBr; 9-C13H9, CH2CH2OH, (m. 143-4), , , , C, 68, 243-4c, C19H22N2O.2HCl; 9-C13H9, 9-C13H9, (m. 291-2)c, , , , A, Quant., , C30H26N2; 9-C14H9CHb, Me, , , , , C, 43, 254-5, C20H22N2.2HCl; 9-C14H9CH2, 9-C14H9CH2, (m. 253-4), , , , A, Quant., 283-6, C34H30N2.2HCl; 2-C5H4N, H, 114-16, 1.4, 1.5888, 27, A, 40, 275-6, C9H13N3.2HCl; 2-C5H4N, Me, 106-7, 2.7, 1.5625, , B, 82, 258-9, C10H15N3.2HCl; 2-C5H4N, 2-C5H4N, 135-40, 1.4, (m. 124-6), A, 15, 281-3, C14H16N4.2HCl; aFluorenyl. bPhenanthryl. cDecompn. dForms a monohydrate, C20H24N2.HCl.H2O, m. 86-7° (from iso-PrOH).

L12 ANSWER 34 OF 36 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1947:27372 CAPLUS
DOCUMENT NUMBER: 41:27372
ORIGINAL REFERENCE NO.: 41:5447d-i,5448a-i,5449a-i,5450a-i,5451a-e
TITLE: Respiratory stimulants. I. Fully substituted ureas derived from α,ω-alkylenediamines
AUTHOR(S): Boon, W. R.
CORPORATE SOURCE: Imperial Chem. Inds. Ltd., Blackley, UK
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AB Aeschlimann (C.A. 31, 2675.3) showed that CO(NEt2)2 and piperazine -1,4-bis(carboxydiethylamide) possessed respiratory-stimulant properties. It was decided, therefore, to examine the reaction between COCl2 and some N,N'-dialkylethylene- or -trimethylenediamines which was expected to give either a 1,3-dialkyl-2-imidazolidone or a bis(carbamyl chloride). (CH2NPhMe)2 (m. 50°) results in 83% yield from 1128 g. (CH2Br)2 and 1819 g. PhNHMe with anhydrous Na2CO3 on stirring 24 h. at 105°. (CH2CH2NPhMe)2 m. 46°, 84%; (CH2CH2NPhEt)2 b16 230°, m. 39°, 85%. N,N'-Diphenyl-N,N'-diisopropylethylenediamine m. 62°, 21%; by heating 17 h. at 120°, the yield is 60%. PhN(CH2CH2OH)Et (247 g.) in 650 cc. PhMe at 2°, added to 190 g. SOCl2 in 100 cc. PhMe and the mixture stirred at room temperature overnight, gives 82.5% PhN(CH2CH2Cl)Et (I), b42 163-4°. PhNHEt and Cl(CH2)3OH give N-ethyl-N-(3-hydroxypropyl)aniline, b16 168-72°; SOCl2 gives 64% N-ethyl-N-(3-chloropropyl)aniline (II), b30 161°. PhNHMe (870 g.) and 393 g. I, heated 16 h. on the steam bath, give 83% PhMeNCH2CH2NPhEt, b16 226-8°, m. 35°; II gives 84% N,N'-diphenyl-N-methyl-N'-ethyltrimethylenediamine, b16 216°. N-Methyl-N-(2-ethoxyethyl)aniline, b23 142°. PhN(CH2CH2OH)2 (271 g.) in 500 cc. PhMe, added (45 min.) to 69 g. Na in 150 cc. PhMe at 100-10°, heated 6 h., the cooled solution treated with 462 g. Me2SO4 (Et2SO4(?)) in 500 cc. PhMe (temperature not above 30°) and stirred 12 h. at room temperature, gives 39% N,N-bis(2-ethoxyethyl)aniline, b25 187-9°.

N,N'-Bis(p-tolylsulfonyl)-N,N'-dialkylalkylenediamines were prepared (A) by adding 2.25 mols. alkyl sulfate or iodide (2 h.) to 1 mol. of N,N'-bis(p-tolylsulfonyl)alkylenediamine in MeOH and 1.1 mols. 32% NaOH, stirring 1 h. at room temperature, and refluxing 4 h., or (B) by adding 1 mol. (CH2)nBr2 to 2 mols. of the Na derivative of N-alkyl-p-toluenesulfonamide (prepared with 2 atoms Na in xylene at 105°, adding 3.2 mols. EtOH, cooling to 60°, adding the amide, and removing the EtOH). (p-Tolylsulfonyl)methylisopropylamine b40 226°, 78°, 89%(B). N,N'-Substituted N,N'-bis(p-tolylsulfonyl)ethylenediamines, (C7H7SO2NRCH2)2 (R given; all prepared by method A): Me m. 164°, 85%; Et m. 158°, 60%; Pr m. 122°, 66%; iso-Pr m. 221°, 87%; allyl m. 146°, 75%; Bu m. 119°, 66%; iso-Bu m. 143°, 19%. N,N'-Bis(p-tolylsulfonyl)trimethylenediamines : Me m. 113°, 50% (A); Et, m. 68° (A); Pr, b0.1 280-90°, m. 47° (B). N,N'-Bis(p-tolylsulfonyl)-N,N'-dimethyltetramethylenediamine m. 131°, 88% (B); the corresponding pentamethylene homolog b0.4 285°, m. 61°, 98% (B); hexamethylene homolog m. 140°, 84% (A); N,N'-bis(p-tolylsulfonyl)-N,N'-diethylhexamethylenediamine m. 115°, 81% (A). N,N'-Dialkylalkylenediamines were prepared by 3 methods: (A) One mol. of the bis(p-tolylsulfonyl) derivative in 8.2 mols. 98% H2SO4, diluted with 9 mols. H2O, and heated 7 h. at 140-5°, cooled, diluted with H2O, made alkaline with 32% NaOH, distilled with steam, the distillate acidified (HCl), evaporated to dryness, and the base liberated with 32% NaOH. (B) (CH2)n(N-Ph-alkyl)2 (1 mol.) in 6.3 mols. concentrated HCl, diluted with 92.5 mols. H2O, is treated with 2.22 mols. aqueous NaNO2, and the precipitated NO compound in 7.5 mols. 20% aqueous NaHSO3 is heated 5 h. at 90-5°. (C) (CH2)nBr2 (1 mol.), 5 mols. primary amine, and 3 mols. H2O are refluxed 15 h., excess 32% NaOH added, the excess primary amine removed by distillation, the residual solution distilled to dryness in vacuo, and the diamine salted from the distillate with solid NaOH. MeNH(CH2)2NHEt b. 135°, 44% (B). N,N'-Disubstituted ethylenediamines: Me, b. 120°, 80% (A), 75% (B), 15% (C); Et, b. 151-2°, 80% (A), 50% (B). Pr, b. 186-9°, 91% (A) (di-HCl salt, m. 300° (decomposition)); iso-Pr, b. 169-71°, 38% (C), 0% by (A) and (B) (di-HCl salt, m. 250° (decomposition)); allyl, b. 198-200°, 41% (C), 0% (A) (di-HCl salt, m. 250° (decomposition)); Bu, b. 226-8°, 80% (A) (di-HCl salt, m. 295-300° (decomposition)); iso-Bu, b. 212-14°, 90% (A), 57% (C) [di-HCl salt, m. 285° (decomposition); Rameau (C.A. 32, 3395.2) gives 130°]; sec-Bu, b. 210°, 51% (C) (di-HCl salt, m. 187°); tert-Bu, b. 196-8°, 42% (C) (di-HCl salt, m. 275-80° (decomposition)); cyclohexyl, b. 312°, 78% (C) (di-HCl salt, m. 312°); 2-methoxyethyl, b. 240-1°, 44% (C) (di-HCl salt, m. 196°); 2-ethoxyethyl, b. 256-8°, 50% (C) (di-HCl salt, m. 212°); 2-isopropoxyethyl, 33% (C) (di-HCl salt, m. 231°). N,N'-Disubstituted triethylenediamines: Me, b. 145°, 80% (B) (di-HCl salt, m. 266°); N-methyl-N'-Et, b. 158°, 72% (B) (di-HCl salt, m. 270°); Et, b. 170-3°, 46% (B) (di-HCl salt, m. above 300°); Pr, b. 212-16°, 68% (A) (di-HCl salt, m. 300°). N,N'-Dimethyltetramethylenediamine, b. 164°, 70% (A) (di-HCl salt, m. 275° (decomposition)). N,N'-Dimethylpentamethylenediamine, b. 190°, 41% (A) (di-HCl salt, m. 254° (decomposition)). N,N'-Dimethylhexamethylenediamine, b. 205°, 80% (A) (di-HCl salt, m. 210°); di-Et homolog, b. 228°, 77% (A) (di-HCl salt, m. 278°); bis(2-ethoxyethyl) analog, b18 190-3°, 30% (C) (di-HCl salt, m. 262° (decomposition)). None of the free bases were analyzed because of their marked tendency to take up H2O and CO2; the HCl salts were analyzed. Me2NCOCl and Et2NCOCl were prepared according to Lumiere and Perrin (Bulletin society chim. 31, 689(1904)), 75% yields being obtained if the amine in PhMe is added to about 3 mols. COCl2 in PhMe at about -10°. 4-Morpholinecarbonyl chloride b33 137-8°; bis(2-ethoxyethyl)carbamyl chloride b19 165°; ethyl(2-ethoxyethyl)carbamyl chloride b20 108°. 2-Alkoxyethylamines were prepared in yields of 65-75% by reduction of the nitriles over Raney Ni; 2-iso-propoxyethylamine b1 116-18° (picrolonate, m. 201-2°), 2-BuO homolog b22 148-50° (picrolonate, m. 172°). PhN(C2H4OMe)Me (165 g.) in 272 cc. concentrated HCl and 500 cc. H2O, treated at 2° or below with 74 g. NaNO2 in 125 cc. H2O, the NO compound added to boiling NaOH (275 g. in 5600 cc. H2O), the distillate acidified with HCl, concentrated to 300 cc., made alkaline with 32% NaOH, and distilled to dryness, gives 51% MeOC2H4NHMe, b1 98-9° (picrolonate, m. 205°); MeOC2H4NHEt forms a picrolonate, m. 222-3°. EtOC2H4NHEt results in 20% yield by the NO method or in 42% yield on heating EtOC2H4NH2 and EtBr with H2O 24 h. at 90-100° (picrolonate, m. 181-2°). PhN(C2H4OEt)2 through the NO derivative yields 27.5% (EtOC2H4)2NH, b. 198-200° (picrolonate, m. 161°); EtOC2H4NH2 (200 g.), 108 g. EtOC2H4Cl, and 25 cc. H2O, refluxed 20 h., give 61%. (CH2NHMe)2 (145 g.) in 500 cc. PhMe, added to 170 g. COCl2 in 1000 cc. PhMe at -15°, gives 24 g. 1,3-dimethyl-2-imidazolidone (III), b15 104°, and a residue of (CH2NMeCOCl)2; di-Et homolog of III b22 122°; di-Pr homolog b23 148°; di(iso-Pr) homolog b15 130°. N,N'-Diisopropylethylenediamine-N,N'-dicarbonyl chloride m. 110°. 1,3-Dimethylhexahydro-2-pyrimidone b44 164°. (CH2NHEt)2 (48 g.) and 50 g. Et2NCOCl in PhMe, mixed below 0° and stirred 1 h., give 14 g. 1,1,3-triethyl-3-(2-ethylaminoethyl)urea, b17 126-8°, and 38 g. N,N'-diethylethylenediamine-N,N'-bis(carboxydiethylamide) b19 218°. 1-Methyl-1,3-diethyl-1-(3-methylaminopropyl) urea (IV) b10 141°; N,N'-dimethyltrimethylenediamine-N,N'-bis-(carboxydiethylamide) (V) b10 210°. 1-Methyl-1,3-diethyl-1-(6-methylaminohexyl)urea b12 182°; N,N'-dimethylhexamethylenediamine-N,N'-bis(carboxydiethylamide) b9 229-30°. 1,1-Pentamethylene-3-(2-ethoxyethyl)-3-[2-(2-ethoxyethylamino)ethyl]urea b15 180°. Bisureas of the type XCONR(CH2)nNR'COX are prepared (A) by adding 5 mols. of a secondary amine to 1 mol. ClOCNR(CH2)nNR'COCl in C6H6 and allowing the mixture to stand overnight; (B) by addition of 1.1 mols. carbamyl chloride to 1 mol. RNH(CH2)nNHR' in C6H6. The new compds. are given in the table. IV (25 g.) and 10 g. 1-piperidinecarbonyl chloride, heated (after initial reaction) 2 h. on the water bath, give 78% N,N'-dimethyltrimethylenediamine-N-carboxydiethylamide-N'-carboxypiperidide, b17 245°, soluble to the extent of 25% in H2O. N,N'-Dimethylhexamethylenediamine-N-carboxydiethylamide-N'-carboxymorpholide b9 248°, 75%, miscible with H2O. N,N'-Bis(2-ethoxyethyl)ethylenediamine-N-carboxydimethyl-XCONR(CH2)nNR'COX; B.p., M.p. yield,; X, R, R', n, Method, t°/mm., t°, %; Me2N, Me, Me, 2, B, 193-5/20, 48; Et2N, Me, Me, 2, A, 224/13, 339, 90; O(CH2CH2)2N, Me, Me, 2, B, 164, 75; Me2N, Me, Et, 2, B, 204-5/22, 72; Et2N, Me, Et, 2, B, 204/10, 67; (CH2)5N, Me, Et, 2, B, 252-4/6, 83; O(CH2 (CH2)2N, Me, Et, 2, B, 76, 50; Me2N, Et, Et, 2, B, 203-5/23, 85; Et2N, Et, Et, 2, B, 226-8/29, 85; (CH2)5N, Et, Et, 2, B, 65, 50; O(CH2CH2)2N, Et, Et, 2, B, 98, 68; MeOC2H4NEt, Et, Et, 2, A, 239-40/17, 75; Me2N, Pr, Pr, 2, B, 208-9/18, 65; O(CH2CH2)2N, Pr, Pr, 2, B, 86, 33; EtOC2H4NMe, Pr, Pr, 2, A, 255/20, 46; MeOC2H4NEt, Pr, Pr, 2, A, 265/20, 58; Me2N, iso-Pr, iso-Pr, 2, B, 202/17, 100, 40; O(CH2CH2)N, iso-Pr, iso-Pr, 2, B, 126, 29; Me2N, allyl, allyl, 2, B, 220/20, 80; O(CH2CH2)2N, allyl, allyl, 2, B, 85, 77; Me2N, Bu, Bu, 2, B, 222-4/18, 68; O(CH2CH2)2N, Bu, Bu, 2, B, 41, 60; (EtOC2H4)2N, Bu, Bu, 2, B, 240-5/12; Me2N, iso-Bu, iso-Bu, 2, B, 220/30, 97; O(CH2CH2)2N, iso-Bu, iso-Bu, 2, B, 270-5/15, 65; Me2N, sec-Bu, sec-Bu, 2, B, 232-4/40, 105, 38; O(CH2CH2)2N, sec-Bu, sec-Bu, 2, B, 135, 30; O(CH2CH2)2N, tert-Bu, tert-Bu, 2, B, 132, 9; O(CH2CH2)2N, cyclohexyl, cyclohexyl, 2, B, 148, 25; Et2N, MeO(CH2)2, MeO(CH2)2, 2, B, 252/23, 50; (CH2)5N, MeO(CH2)2, MeO(CH2)2, 2, B, 285/17, 54; O(CH2CH2)2N, iso-PrO(CH2)2, iso-PrO(CH2)2, 2, B, 94, 53; Me2N, Me, Me, 3, B, 213/24, 56; Et2N, Me, Me, 3, B, 225/21, 88; NMePr, Me, Me, 3, A,

225/16, 57; NMe(iso-Pr), Me, Me, 3, A, 218/15, 60; (CH2)5N, Me, Me, 3, B, 205/0.75, 73; O(CH2CH2)2N, Me, Me, 3, B, 93, 60; MeOC2H4NMe, Me, Me, 3, A, 253/16, 61; EtOC2H4NEt, Me, Me, 3, A, 258/15, 61; MeOC2H4NEt, Me, Me, 3, A, 254/19, 61; EtOC2H4NEt, Me, Me, 3, A, 253/14, 49; Me2N, Me, Et, 3, B, 219/21, 84; N,N'-Bis(2-ethoxyethyl)ethylenediamine-N- carboxy [ethyl(2-ethoxyethyl)]amide-N'- carboxypiperidide b10 245-7°, 21%, miscible with H2O. In the series of compds. of the general formula XCONR(CH2)nNR'COY, lengthening the hydrocarbon chain between the diamine N atoms increases the activity if X, Y, R, and R' are kept constant but the solubility in H2O is decreased and the toxicity is raised.

The nature of R and R' has a very pronounced effect on the activity; in general, a regular increase occurs from Me to Bu; branching of the chain, unsatn., or the introduction of ether linkages reduces the activity. In the series (CH2)n[NRCON(CH2CH2)2O]2 (VI), activity increases in the order R = Me = CMe3 = CHMeEt < Et < CHMe2 < CH2CH:CH2 < CH2CHMe2 < Pr < Bu. In sym. compds., where X = Y, the degree of activity is generally in the following order: NMeC2H4OMe < NMe2 < O(CH2CH2)2N < NMeC2H4OEt < NEtC2H4OMe < NEtC2H4OEt < NMeCHMe2 < NEt2 < NC5H10. Unsym. compds., in general, possess the mean of the activities of the 2 related sym. compds. Certain exceptions are noted. However, the value of a compound depends more on a suitable balancing of different groups within the mol. The most active compds. appear to be those which are distributed approx. equally between H2O and hydrocarbon solvents. In VI, if R is Me or Et, the products have very high H2O solubility with low solubility in hydrocarbon solvents and low respiratory-stimulant activity; if R is Pr or Bu, the solubility in hydrocarbon solvents increases and very potent stimulants are obtained, with approx. 12 times the activity of nikethamide (VII). The 2 most interesting compds. with a short duration of action are V and N,N'-dipropylethylenediamine-N,N'-bis(carboxydimethylamide), which are approx. twice as active as VII; whereas the ratio of convulsant dose to stimulant dose is 7.5 in the case of V as compared with 2.8 for VII, the 2nd compound is devoid of convulsant action. Both compds., unlike VII, can be administered repeatedly without habituation. By the continuous administration of a suitable mixture of a short-acting barbituric acid derivative (e.g., hexobarbitone) and either of these compds., it is possible to maintain an animal under anesthesia with its respiratory activity at the normal conscious level.

L12 ANSWER 35 OF 36 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1937:8813 CAPLUS
DOCUMENT NUMBER: 31:8813
ORIGINAL REFERENCE NO.: 31:1164d-h
TITLE: Antimony compounds of polyhydroxy carboxylic acids
INVENTOR(S): Schmidt, Hans
PATENT ASSIGNEE(S): Winthrop Chemical Co.
DOCUMENT TYPE: Patent
LANGUAGE: Unavailable
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2066742		19370105	US 1930-500434	19301205

AB By the reaction of gluconic, saccharic, mucic, galactonic, mannonic or quinic acid with trivalent Sb compds. such as oxide, hydroxide or halide (suitably with an alc. and water as solvents of the initial reacting compds.) and neutralizing the reaction product with an alkali such as dilute NaOH solution, complex compds. are obtained suitable for therapeutic use by injection or for use as intermediate products, etc., and which are generally colorless powders dissolving in water with a neutral reaction. The reacting materials may be heated on a water bath, and the process is stated to relate generally to processes by which neutral water-soluble complex salts of trivalent Sb with a saturated, aliphatic or alicyclic polyhydroxy carboxylic acid, containing at least 5 C atoms and 3 OH groups bound to 3 adjoining C atoms, are obtainable by reacting upon a preferably aqueous or aqueous-alc. solution of the acid with a trivalent Sb compound, such as Sb oxide, hydroxide or mineral acid salts thereof, e. g., Sb sulfate, or SbCl3, SbBr3 or SbF3, and neutralizing the reaction mixture with a basically reacting substance. As polyhydroxy carboxylic acids of the said kind preferably the acids obtainable by oxidation of carbohydrates have proved suitable, e. g., polyhydroxy carboxylic acids of the pentane and hexane series, such as pentonic acids, e. g., arabonic-, xylonic-, and 2-methylpentane-tetrolic acid, hexonic acids, e. g., gluconic, galactonic, mannonic and talonic acid, trihydroxy glutaric acids, tetrahydroxy adipic acids, e. g., saccharic-, iso-saccharic-, mucic- and manno-saccharic acid, etc.; also acids derived from disaccharoses which contain 2 polyhydroxy hexane residues combined with an ether-like bound O atom., e. g., lactobionic acid; also alicyclic polyhydroxy carboxylic acids containing at least 3 OH groups bound to 3 adjoining C atoms, for instance, quinic acid. As bases for the neutralizing process, alkalies, preferably alkali metal hydroxides or N bases, such as NH3, mono-, di- and tri-ethylamine, ethylenediamine, diethylaminoethanol and piperazine are suitable.

L12 ANSWER 36 OF 36 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1907:9334 CAPLUS
DOCUMENT NUMBER: 1:9334
ORIGINAL REFERENCE NO.: 1:2243e-i,2244a-e
TITLE: The Action of Sulphites on Aromatic Amino and Hydroxy Compounds
AUTHOR(S): Bucherer, Hans Th.; Leyde, Franz
CORPORATE SOURCE: Lab. Tech. Hochschule, Dresden
SOURCE: Journal de Physiologie (Paris, 1946-1992) (1907), 75, 249-93
CODEN: JOPHAN; ISSN: 0021-7948
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AB In a previous contribution (Ibid., 70, 362). it was shown that secondary and tertiary amines are decomposed by boiling sulphite solution thus: RNHR, or RN(R)2 → ROH RNH2 or NH(R1)2. The preparation of benzylamine dibenzylamine and piperazine by this method was attempted; only benzylamine was obtained with satisfactory yields. Benzyl chloride was first condensed with 1,4-naphthylamine-sulphonic acid by means of sodium carbonate, yielding 71% of benzylnaphthionic acid, light yellow needles. When sodium acetate instead of sodium carbonate was used, a by-product was formed-dibenzyl-α-naphthylamine, white needles, m. 108°, its alcoholic solution fluoresces blue; with HCl it forms a crys alline hydrochloride, m. 186°, easily decomposed by water. With 1,4,7- and 1,4,8-naphthylaminedisulphonic acids and benzyl chloride, the corresponding monobenzyl compounds were obtained. Upon boiling these monobenzylnaphthalene acids with an excess of bisulphite 70-75% yields of benzylamine were obtained; the higher benzylated acids gave only 12-20% yields of benzylamine. A number of aryl derivatives of β-naphthylamine were prepared by boiling naphthalenesulphonic acids with primary amines in the presence of an excess of bisulphite solution. β;-Naphthol-6,8-disulphonic acid with p-phenylenediamine gave 82% of p-aminophenyl-β-naphthylamine-6,8-disulphonic acid, yellow microcrystalline needles; with p-aminophenyl it gave 84% of p-hydroxyphenyl-β-naphthylamine-6,8-disulphonic acid, white-yellow needles. The 2,3-hydroxynaphthoic acid was condensed with a large number of primary amines; C10H6(OH)COOH+H2NC6H4CH3 → C10H7NHC6H6CH3+H2O+CO2. p-Toluidine gave p-tolyl-β-naphthylamine (82%), glistening white leaflets, from alcohol, m. 102°-103°; m-toluidine gave m-tolyl-β-naphthylamine (34%), white needles, m. 67°-68°, soluble in most organic solvents;

o-toluidine gave o-tolyl-β-naphthylamine (28%), m. 105°; m-xylidine gave m-xylyl-β-naphthylamine, large transparent rhombic prisms, from ligroin, m. 40°; p-anisidine gave p-methoxyphenyl-β-naphthylamine (74%), rhombic leaflets, from ligroin, m. 104°; o-anisidine gave o-methoxyphenyl-β-naphthylamine (27%), leaflets m. 68°; p-phenetidine gave p-ethoxyphenyl-β-naphthylamine (61%), white leaflets, m. 95°, m-toluylenediamine gave m-aminotolyl-β-naphthylamine (55%), red, crystalline powder, m. 95°; hydrochloride, m. 205°; p-phenylenediamine gave p-aminophenyl-2-aminonaphthalene (64%), glistening needles, m. 94°; monohydrochloride, colorless needles, m. 270°; dihydrochloride, m. 270°; acetyl compound, m. 160°; o-aminobenzoic acid gave naphthylanthranilic acid (17%), brown, amorphous powder; aminosalicylic acid gave β-naphthyl-5-amino-o-hydroxybenzoic acid, yellow needles or leaflets, m. 176°; metanilic acid gave phenyl-β-naphthylamine-3-sulphonic acid, white needles; sulphanilic acid gave phenyl-β-naphthylamine-4-sulphonic acid; pararosaniline gave naphthyl-fuchsine, a green crystalline mass, evidently a mixture; safranine gave naphthylsafranine, glistening green crystals, a mixture. Nigrotinic acid (2,8)-dihydroxynaphthalene-3-carboxyl-6-sulphonic acid (Ber., 26, 1119) and p-toluidine gave p-tolyl-2-amine-8-naphthol-6-sulphonic acid. The constitution of nigrotinic acid was established. It was purified through its o-toluidine salt and the latter decomposed by concentrated HCl yielding 67% of the pure acid. Upon boiling the acid with p-toluidine and bisulphate, it yielded p-tolyl-γ-acid, (2,8)(OH)2C10H5SO3H(6). Upon heating with ammonium sulphite and ammonia at 150°, it yielded 59% of 2-amino-8-hydroxynaphthalene-6-sulphonic acid (J. pr. Chemical, 69, 79).

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